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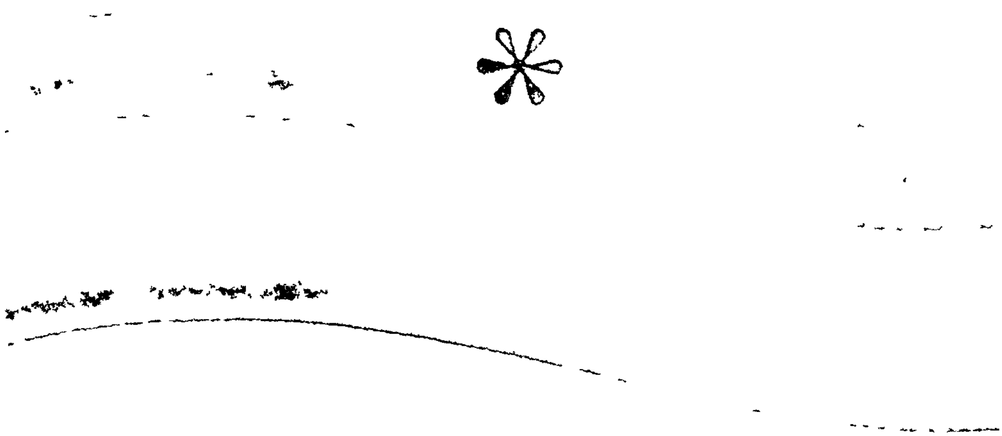

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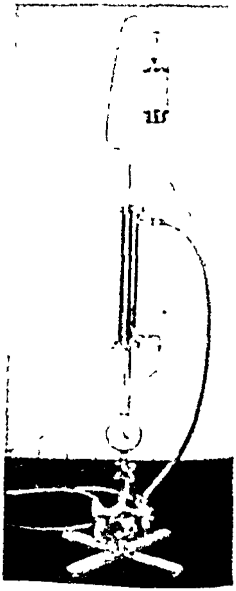

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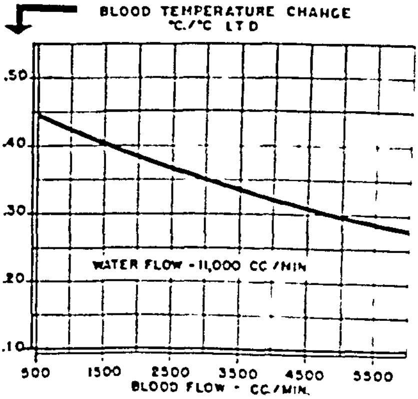

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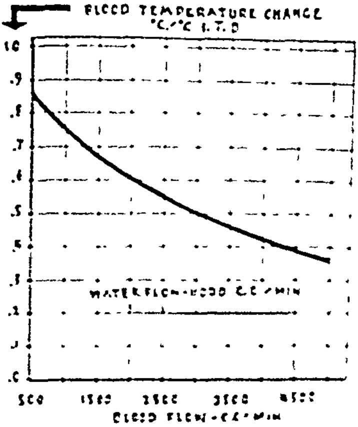

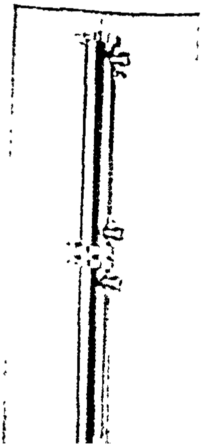

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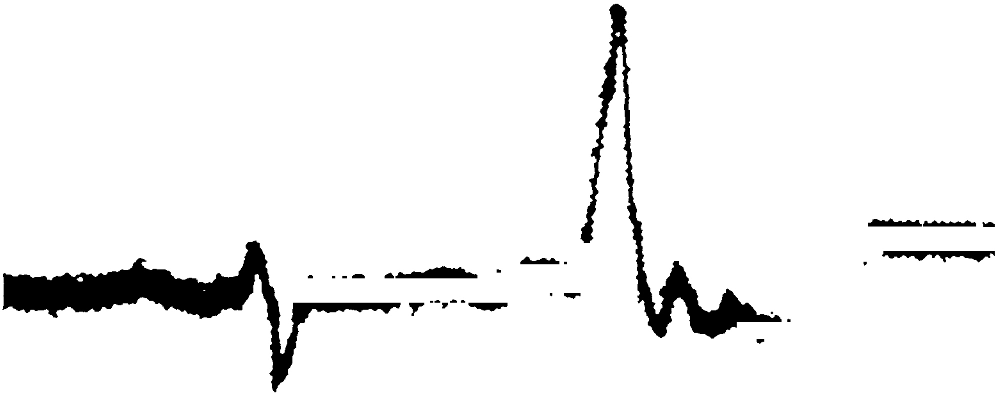

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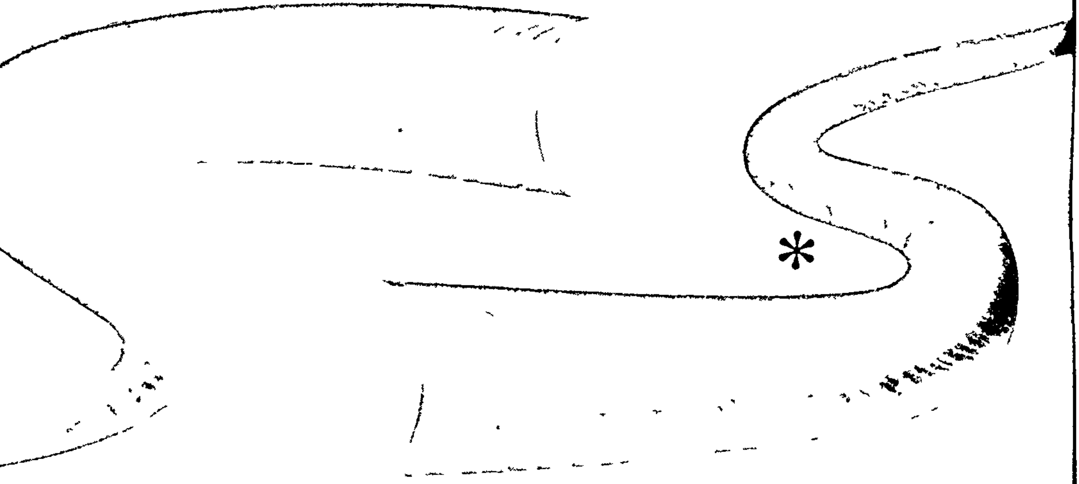

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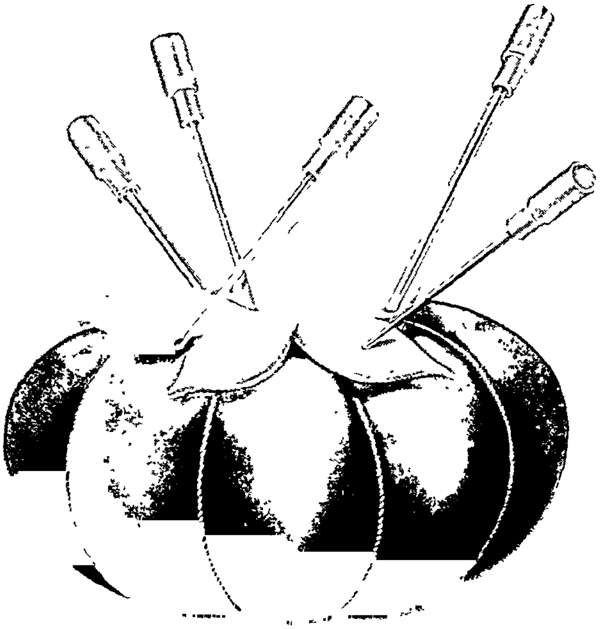

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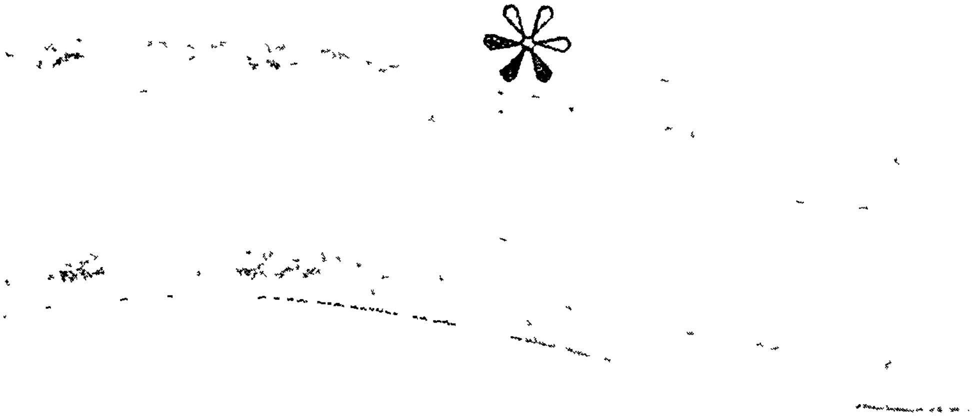

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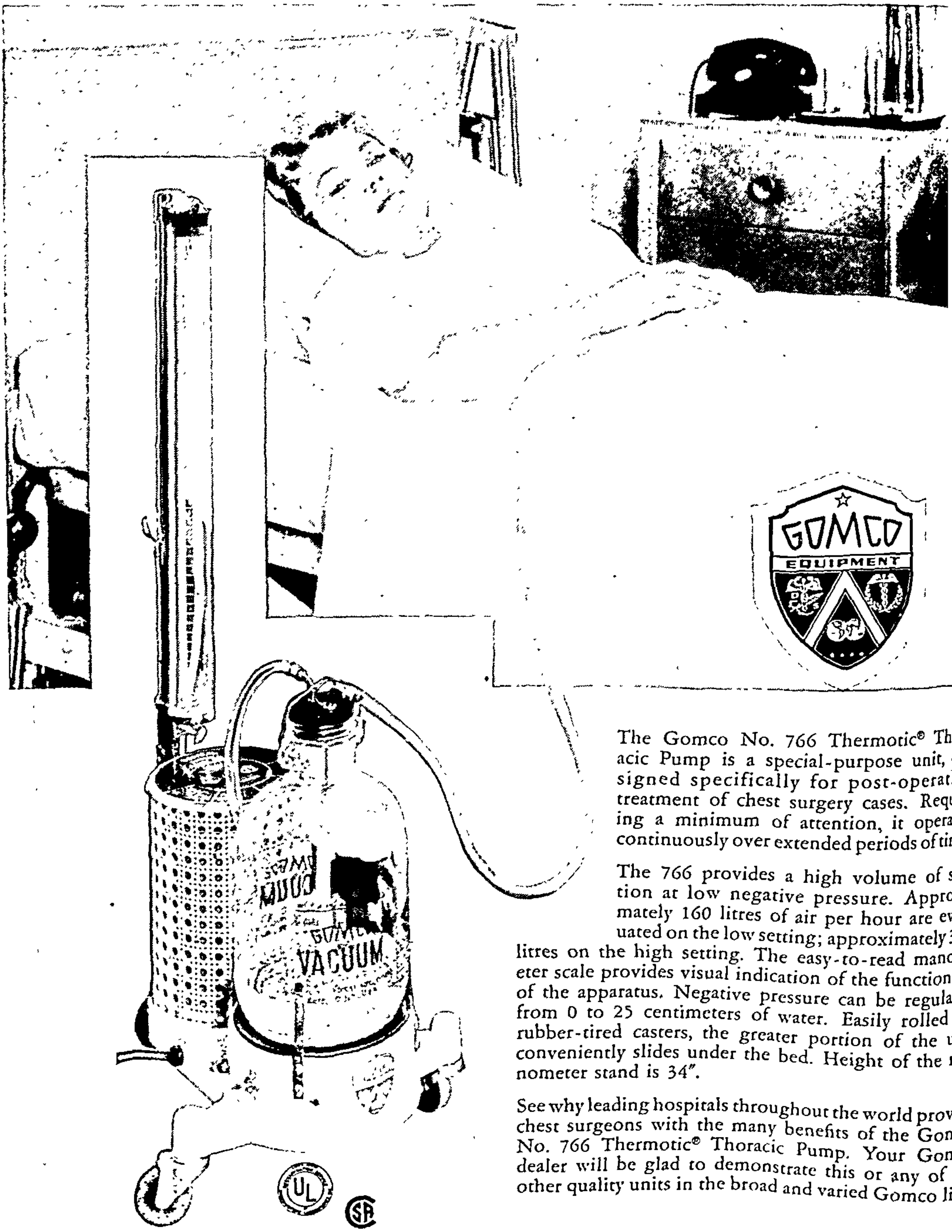

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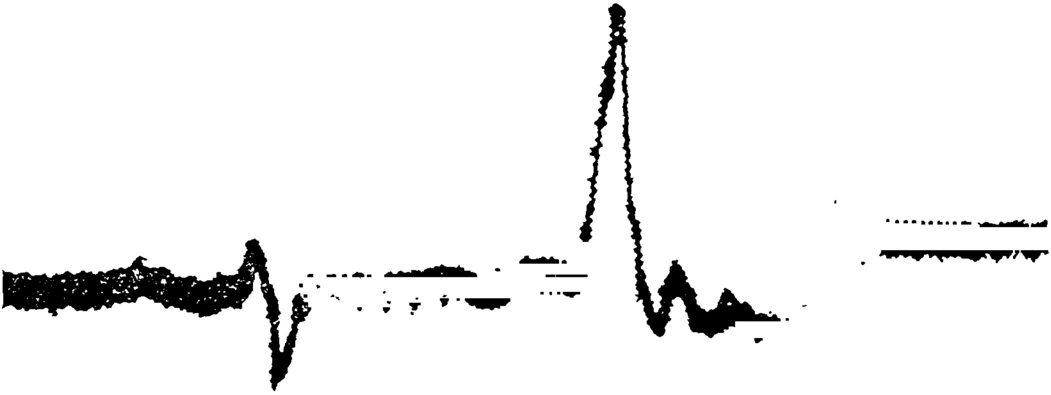

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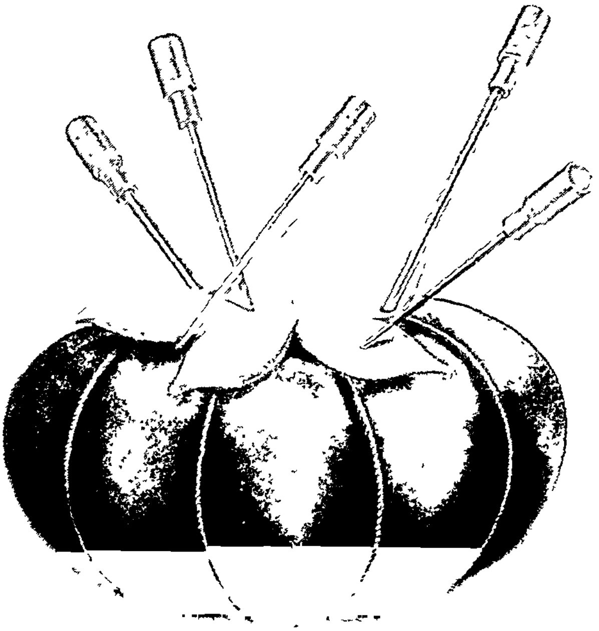

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MAYO PROFOUND HYPOTHERMIA APPARATUS and the IBM-MAYO INTRACARDIAC SUCKER SYSTEM

The **MAYO PROFOUND HYPOTHERMIA APPARATUS** was developed in cooperation with Mayo Clinic and is used to induce and reverse profound hypothermia by right and left by-pass. This apparatus has been in use clinically and was exhibited at the Florida Thoracic Meeting. It consists of two constant volume reservoir and blood pump systems, heat exchanger, filling reservoir and arterial filter. The pumps are of the new Mayo single roller design and run totally occlusive. The apparatus is designed to operate automatically or under manual control. A principal object of the design is to minimize the priming volume. The following features are included:

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Arterial filter serves as bubble trap
Separate ice bucket cart and circulating pump
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Height indicator calibrated with reference to suction at patient's atrium
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Standard apparatus operates on 115 volts, 60 cycles

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and the femoral artery, complete cardiopulmonary bypass was instituted, the left atrium was opened widely and the mitral valve was excised. The prosthesis was then inserted in the manner described and illustrated later. After the atriotomy had been closed and bypass discontinued, the competency of the valve was assessed by measurements of left atrial pressure and the tension on the chordae was adjusted (Fig. 4). A mean left atrial pressure of 8 to 12 mm. Hg was considered evidence of satisfactory valve function when systemic arterial pressure was normal, and this level of atrial pressure was achieved in six of the last ten experiments.

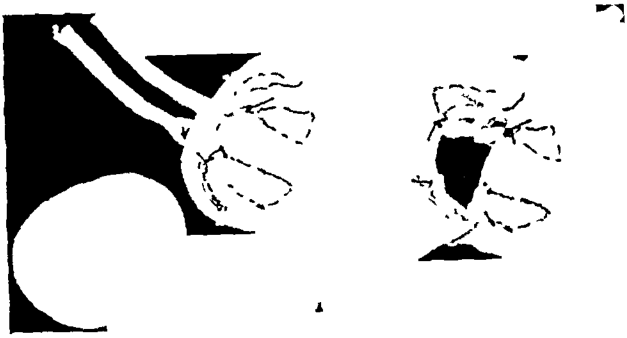

Fig 3—The completed valve before (*left*) and after (*right*) incision of the commissures and attachment of the chordae.

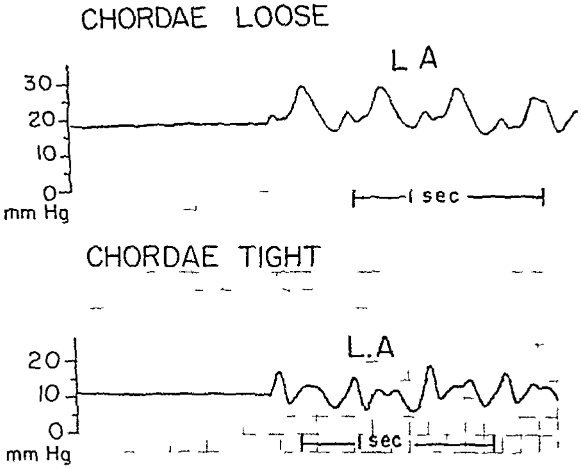

Fig 4—Left atrial pressure tracings obtained in an experimental animal before and after adjustment of the tension on the chordae of the prosthetic valve

In the initial experiments no systematic attempt was made to obtain survival since not only were valves of various designs employed but the technique of insertion was also modified continually. In more recent operations, when the design of the valve and surgical technique had been standardized, chronic survival was still not achieved but 4 dogs lived from 8 to 40 hours. In them, autopsy revealed that the valve surface was covered with a thin layer of fibrin but clot formation was never observed; there was no evidence that death would be most likely to provide an effective functional substitute. Such a design takes advantage of ventricular contraction as well as the pressure differences between the atrium and ventricle. Wax or plaster casts were made of the mitral ring and the mitral valve leaflets in fresh normal or diseased human hearts and in the hearts of normal dogs and calves (Fig. 1). The casts were trimmed and smoothed and from them two-piece molds were made of Devcon, an industrial molding compound* (Fig. 2). In constructing the valve, a thin piece of knitted Dacron fabric was stretched over the male half of the mold and secured around its base. The female half of the mold was then half-filled with catalyzed liquid polyurethane† and the mold was quickly closed and compressed. The valve was cured in the mold overnight, then removed and trimmed. The valve orifice was cut and "chordae tendineae" of Teflon tape were sutured to the leaflets as shown in Fig. 3.

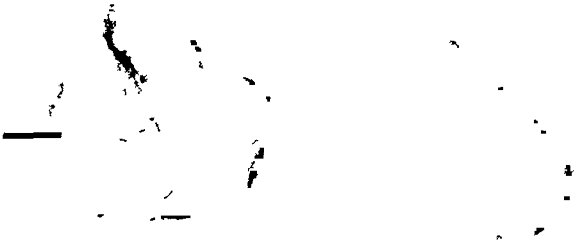

Fig 1.—Plaster *(left)* and wax *(right)* casts of the mitral valve made at autopsy

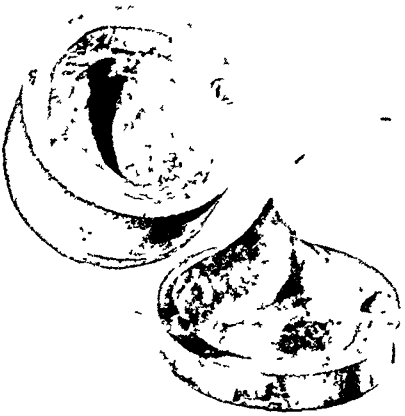

Fig. 2—A completed mold in which the valve is fabricated

Valves constructed in the manner described were used for complete replacement of the mitral valve in 27 dogs A left thoracotomy was made since it was found that the small left atrium of the normal dog could be incised more widely from this approach. After cannulation of the jugular and femoral veins and the femoral artery, complete cardiopulmonary bypass was instituted, the left atrium was opened widely and the mitral valve was excised. The prosthesis was then inserted in the manner described and illustrated later. After the atriotomy had been closed and bypass discontinued, the competency of the valve was assessed by measurements of left atrial pressure and the tension on the chordae was adjusted (Fig. 4). A mean left atrial pressure of 8 to 12 mm. Hg was considered evidence of satisfactory valve function when systemic arterial pressure was normal, and this level of atrial pressure was achieved in six of the last ten experiments.

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*Manufactured by the Devcon Corporation, Danvers, Mass

†Manufactured by American Latex Company, Hawthorne, Calif

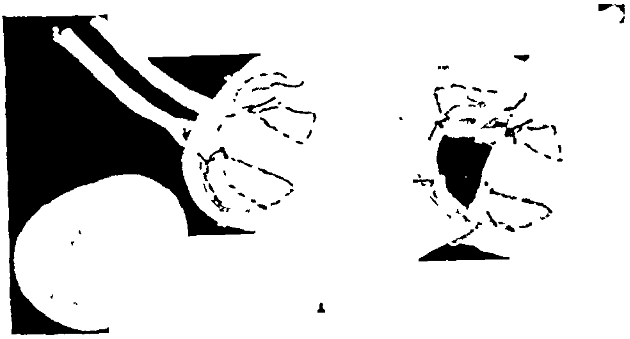

Fig. 3.—The completed valve before *(left)* and after *(right)* incision of the commissures and attachment of the chordae.

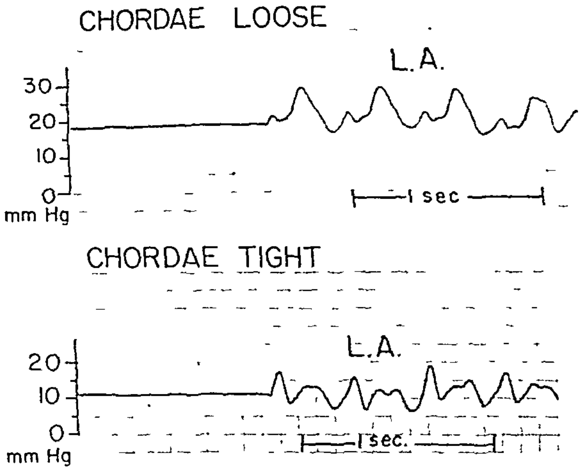

Fig 4.—Left atrial pressure tracings obtained in an experimental animal before and after adjustment of the tension on the chordae of the prosthetic valve.

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In spite of the difficulties described, it was considered that the basic objective, a satisfactory prosthetic valve, had been achieved and experience with reconstructive operations indicated that the technical problems of its insertion in patients would be far simpler than in the normal dog.

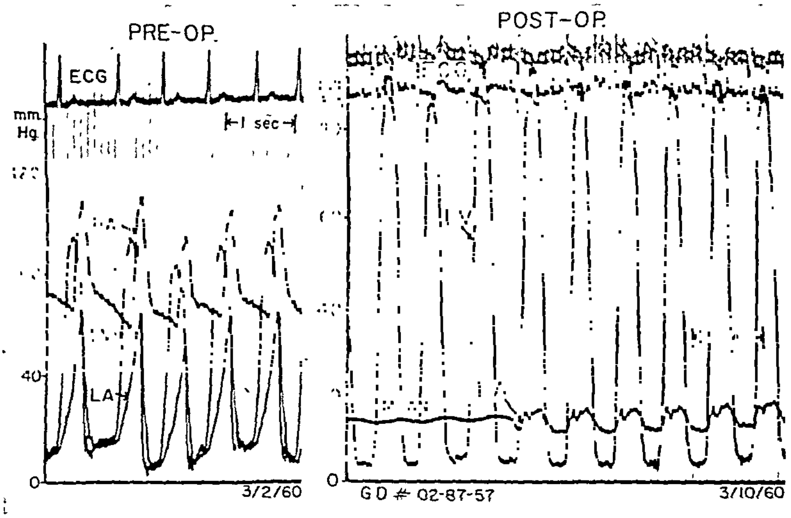

Fig. 5.—Records of left atrial *(LA)*, left ventricular *(LV)*, and brachial arterial *(BA)* pressures obtained in patient G. D. at preoperative catheterization *(left)* and after insertion of the prosthetic valve *(right)*.

CLINICAL APPLICATION

The prosthesis described has been employed in 2 patients for complete mitral valve replacement.

Case 1.—G. D. was a 16-year-old schoolgirl in whom no history of rheumatic fever was obtained. She had been relatively well until 2 years before admission when she began to experience dyspnea, fatigability, and ankle edema. All of these symptoms progressed and she had been hospitalized on several occasions in congestive heart failure. There was a prominent left ventricular lift and a systolic thrill at the apex. A Grade 4/6 systolic murmur was audible over the whole precordium, maximal at the apex and referred to the axilla. No diastolic murmur was present. The chest roentgenogram showed gross cardiac enlargement with prominence of the left ventricle and a greatly dilated left atrium. The electrocardiogram revealed atrial fibrillation.

Combined right and transseptal left heart catheterization showed the right ventricular pressure to be elevated (52/10 mm. Hg). The Kr^{85} test of 2.6 per cent in this chamber excluded a left-to-right shunt. The mean left atrial pressure was 27 mm. Hg and peaks of the v waves were 50 to 60 mm. Hg. There was no diastolic gradient across the mitral valve (Fig. 5).

At operation (March 10, 1960) the anterior leaflet of the mitral valve was found to be contracted, deformed, and extensively scarred. Both leaflets were excised and the prosthesis inserted. Bleeding from a tear in the left atrial suture line necessitated prolonged partial cardiopulmonary bypass until it could be controlled. At the conclusion of the procedure, simultaneous measurements revealed a satisfactory reduction in mean left atrial pressure and a small mitral diastolic gradient (Fig. 5). Palpation of the functioning valve revealed it to be mobile and only a slight regurgitant jet could be felt, apparently localized to the posterior commissure.

Postoperatively the patient reacted promptly, was alert and maintained a normal blood pressure without support. The cardiac rhythm spontaneously reverted to a sinus mechanism. Only a faintly audible systolic murmur was present. After the first 2 hours, however, she became oliguric and the serum potassium, in spite of treatment, rose to 7.3 mEq. per liter. She suddenly became hypotensive and died 60 hours after operation.

At autopsy the valve was found to be in good position and its atrial surface showed no fibrin or clot. Inspection from the ventricular aspect revealed that in placement of the artificial chordae, one had inadvertently been passed behind the other. This had resulted in obstruction to the valve opening where the chordae crossed. A fibrin clot occupied this area.

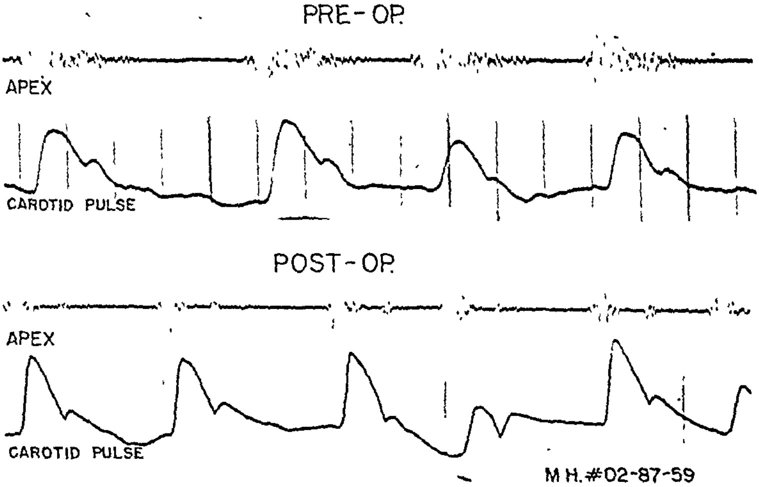

Fig. 6.—Phonocardiograms recorded at the apex of the heart in patient M. H. before and after operation. No systolic murmur is audible or recorded after insertion of the prosthesis.

Case 2.—M. H. is a 44-year-old housewife in whom a heart murmur and cardiac enlargement had been noted since the age of 8 years. There was no history of rheumatic fever. She had had dyspnea and fatigability for many years and since a pregnancy in 1943 all her symptoms had progressed. Six months before admission, congestive failure, edema, orthopnea, and pleural effusion had necessitated hospitalization.

She was thin and appeared chronically ill. The neck veins were dilated, the blood pressure was 110/70 mm. Hg and the pulse completely irregular at a rate of 70 to 80. Numerous crackling râles were heard at both lung bases. The heart was enlarged, the apical impulse lying in the seventh intercostal space outside the anterior axillary line. Both left and right ventricular lifts were palpable and a systolic thrill was present at the apex. The pulmonary second sound was increased but normally split. A Grade 5/6 pansystolic murmur was present at the apex and radiated to the axilla (Fig. 6). A Grade 2/6 diastolic murmur was heard in this area also. The edge of the liver was palpable 6 cm. below the right costal margin. The chest roentgenogram (Fig. 7) demonstrated gross cardiac enlargement with prominence of the left ventricle, left atrium, and pulmonary artery. There was considerable pulmonary congestion. The electrocardiogram showed atrial fibrillation, right axis deviation, and nonspecific S-T segment and T-wave changes, as well as digitalis effect.

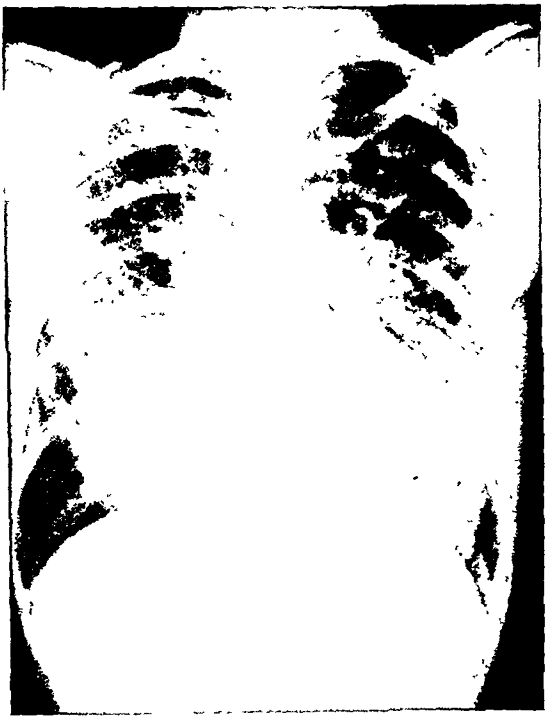

Fig. 7.—Preoperative roentgenographic appearance of heart in patient M. H.

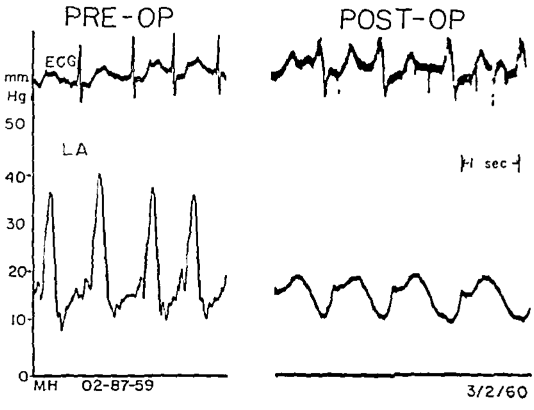

Fig. 8.—Records of left atrial pressure obtained at preoperative catheterization *(left)* and after the insertion of the prosthesis *(right)* in patient M. H.

At right heart catheterization the right ventricular pressure was elevated to 55/10 mm. Hg and the right atrial mean pressure was 11 mm. Hg. Unexpectedly, a small left-to-right shunt entering the right atrium was demonstrated by inhaled Kr^{85} tests. The catheter was then passed across an interatrial communication and into the left ventricle. Arterial indicator dilution curves recorded after left ventricular injection demonstrated a prolonged descent compatible with valvular regurgitation. The left atrial mean pressure was 20 mm. Hg and the pulse contour was that of gross mitral regurgitation (Fig. 8). There was no diastolic gradient across the mitral valve. When the catheter was withdrawn across the interatrial septum a distinct pressure gradient between the left and right atria was recorded.

It was considered that the patient had either an incomplete form of persistent atrioventricular canal or a small atrial septal defect of the usual type with rheumatic mitral regurgitation. At operation (March 11, 1960) palpation of the interatrial septum revealed a small defect in the region of the foramen ovale. Palpation within the left atrium disclosed gross mitral regurgitation through a scarred and thickened valve. There was no calcification. The valve lesion was considered to be of rheumatic rather than of congenital origin. A left atriotomy was made and the anterior leaflet was seen to be curled, thickened, and scarred; the posterior leaflet was rolled and immobile. Both leaflets and their attachments to the papillary muscles were excised. The chordae of the prosthetic valve were placed and the valve sutured to the thickened annulus. The interatrial septal defect, which was 1.5 cm. in diameter, was closed with several interrupted sutures. When left ventricular output had been restored the chordae were adjusted in length until no regurgitant jet could be felt. Pressure measurements after the repair (Fig. 8) showed a small diastolic gradient across the valve but the pulse contour characteristic of mitral regurgitation was absent.

Postoperatively an elective tracheostomy was performed. The patient's blood pressure was supported by small doses of Aramine for 24 hours, after which this was unnecessary. She has made a slow but uneventful recovery and is apparently well 6 weeks after operation. No precordial murmur is audible (Fig. 6).

SURGICAL TECHNIQUE

The operative method employed in each patient was similar. The patient is positioned supine with the right chest elevated to 30-40 degrees and a bilateral anterior thoracotomy is made extending over the right fifth intercostal space and toward the apex of the heart in the left sixth interspace (Fig. 9). Tapes are passed about the venae cavae and the aorta freed from the pulmonary artery to permit occlusion if necessary. The anterior wall of the left atrium is dissected from the right atrium if a large area of it is not evident. After cannulation of the venae cavae and femoral artery, bypass is instituted and a left atriotomy made (Fig. 10). The mitral valve is grasped and excised from the papillary muscles and annulus; a rim of valve tissue, 2 to 3 mm. in width, is left attached to the annulus. The anterior chorda of the prosthetic valve is threaded to a Reverdin needle and passed from the cavity of the left ventricle through its wall near the base of the anterior papillary muscle, the point of the needle being directed so that major coronary vessels are avoided (Fig. 11). The posterior chorda is similarly inserted through the ventricular wall near the base of the posterior papillary muscle. Each chorda is held with a clamp and a mattress suture of heavy silk placed and tied about the site of exit from the heart. The valve is then drawn into position and its commissures carefully aligned as the natural ones were. The free margin of the valve is then anchored with mattress sutures placed in four quadrants of the annulus and the fixation completed with continuous sutures between these points (Fig. 12). After the air has been evacuated from the heart the left atrium is closed with a continuous everting mattress suture except for an area in the center of the suture line

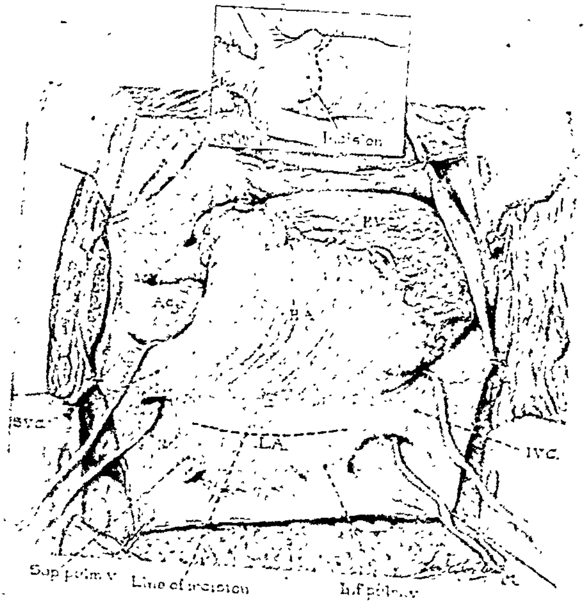

Fig. 9.—Operative exposure employed in mitral valve replacement.

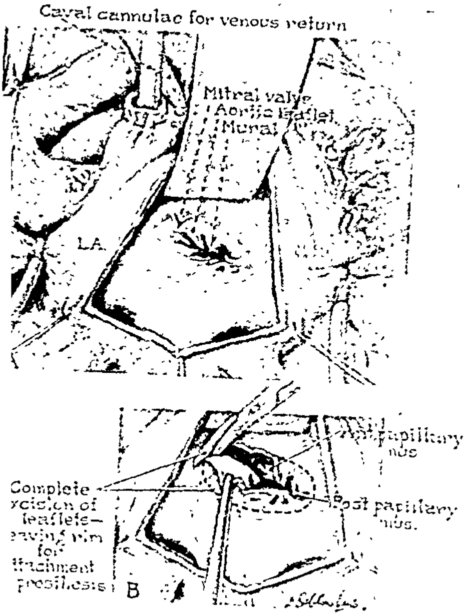
Caval cannulae for venous return
Mitral valve
Aortic leaflet
Mural
LA
Ant. papillary mus.
Post. papillary mus.
Complete excision of leaflets—leaving rim for attachment prosthesis
B

Fig. 10.

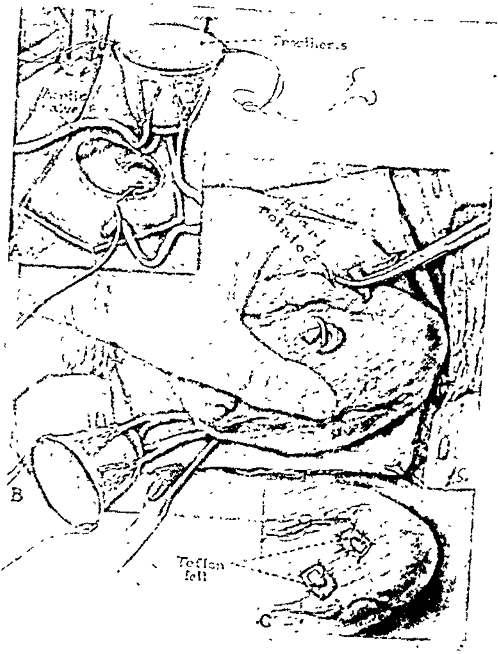

Fig. 11.

Fig. 10.—After total cardiopulmonary bypass has been established the valve is exposed excised as shown.

Fig. 11.—Methods by which the artificial chordae tendineae are placed and later secured he left ventricular wall.

where interrupted sutures are placed but not tied. The finger is inserted through this opening and the vena cava tourniquets are loosened, permitting approximately half the systemic venous return to enter the heart. The length of each chorda is then adjusted until, by palpation, the valve is made maximally competent. They are fixed in this position to the left ventricular wall, buttressed by squares of Teflon felt. The final position of the prosthesis is shown in Fig. 13.

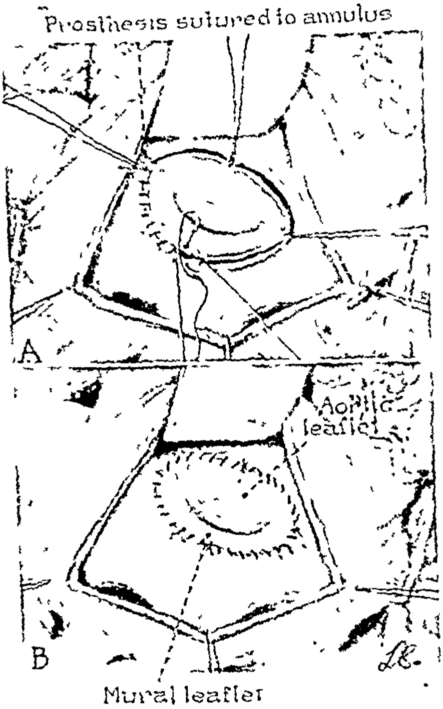

Fig 12.

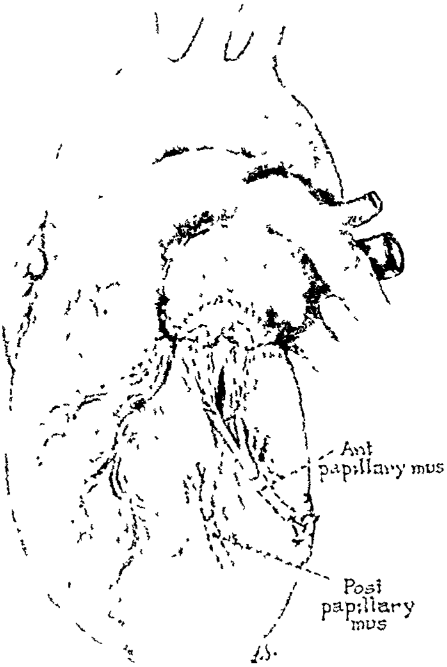

Fig 13

Fig. 12.—Fixation of the prosthesis to the mitral annulus
Fig. 13 —Final position and appearance of the prosthesis after insertion

COMMENT

In the design of the prosthetic valve described, it was considered that the degree of flexibility of the leaflets was of prime importance. When they were made too rigid not only was a relatively high pressure required to open the valve, but there was sufficient resistance to closure in systole so that regurgitation occurred. The extreme flexibility finally achieved precluded any form of internal fixation to prevent leaflet eversion and necessitated the artificial chordae tendineae employed. Early experience with the valve indicated that the length of the chordae was critical and that it was difficult if not impossible to correctly estimate their optimal length when they were sutured to the papillary muscles or ventricle before the valve itself was inserted and functioning. For this reason the chordae were brought through the ventricular wall, adjusted and fixed in the manner described. This technique permits regulation of the tension on the chordae when the ventricle is effectively contracting and, by palpation, optimum competency can be obtained.

Many plastic materials were evaluated in the fabrication of valves. The open-cell polyurethane foam surface eventually employed was selected because it had been shown to be nontoxic and to induce a minimal inflammatory response.[5, 6] It was also considered that its structure would allow tissue ingrowth and eventual formation of an endothelial-like surface. The material has the additional advantage that it can be molded easily without special equipment.

In each of the patients in whom the valve was inserted a small diastolic pressure gradient was present afterward. This observation has suggested certain changes in the design of the valve which should further improve its hemodynamic function. Preliminary studies indicate that a prosthesis molded with the leaflets in a more closed position may be preferable. This modification, which results in a relatively larger anterior or aortic leaflet, also permits a larger orifice to be made without regurgitation. In the surviving patient the left atrial pressures recorded before and after operation do not necessarily reflect the degree of hemodynamic improvement. Before operation an atrial septal defect was present; this communication served to decompress the left atrium and had it not been present the left atrial pressure would undoubtedly have been higher preoperatively.

SUMMARY

Prosthetic mitral valves, designed to simulate the normal valve, have been constructed of an open-cell polyurethane foam reinforced with Dacron fabric. The leaflets are controlled by artificial chordae tendineae which are brought through the wall of the left ventricle, the length of the chordae can be adjusted to provide optimum competency of the valve. After experimental evaluation the prosthesis was employed for complete replacement of the mitral valve in 2 patients, 1 of whom survived. These patients are described and the details of the design and fabrication of the valve and the technique of insertion are presented.

ADDENDUM

May 23, 1960.—The surviving patient remains well following discharge from the hospital. In the fifth postoperative week she developed fever but repeated blood cultures showed no growth and the fever subsided promptly after the administration of penicillin and streptomycin. At this time a faint apical systolic murmur is audible.

REFERENCES

1. Akutsu, T., Dreyer, B., and Kolff, W.: Polyurethane Artificial Heart Valves in Animals, J. Appl. Physiol. 14: 1045, 1959.

2. Ellis, F. H., Jr., and Bulbulian, A.: Prosthetic Replacement Mitral Valve. Preliminary Experimental Observations, Proc. Staff Meet. Mayo Clin. 33: 532, 1958.
3. Wickle, J. H., Jacobson, L. F., Jordan, P. Jr., Johnston, C. G., and Hellers, H. K.: Spring Valve Mitral Prosthesis. Report of One Case With One Year Follow Up, J. Michigan M. Soc. 56: 731, 1957.
4. Kay, E. B., Nogueira, C., and Zimmerman, H. A.: Correction of Mitral Insufficiency Under Direct Vision. Circulation 21: 568, 1960.
5. Salvatore, J. E., and Mandarino, M. P.: Polyurethane Polymer, Its Use in Osseous Lesions: An Experimental Study, Ann. Surg. 149: 107, 1959.
6. Dreyer, B., Akutsu, T., and Kolff, W. J.: Aortic Grafts of Polyurethane in Dogs, J. Appl. Physiol. 15: 18, 1960.

PARTIAL REPLACEMENT OF THE MITRAL VALVE WITH SYNTHETIC FABRIC

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Joe G. Jontz, M.D., Indianapolis, Ind.

INTRODUCTION

As the technique of the open approach for visual correction of mitral valve disease becomes better developed, it is evident that direct plastic reconstruction of the valve leaflet would often be desirable. In many instances the use of foreign tissues or materials would be necessary to restore the valve to a more normal anatomic state. The easy availability of synthetic fabrics would make their use desirable in this location. Whether healing would occur and good function result when plastic cloth was substituted for part of an actively moving valve, subjected to high pressure changes, was not known. The present study was therefore undertaken.

METHODS

Mongrel dogs weighing 11 to 18 Kg. were used. Anesthesia was induced and maintained with intravenous methohexital sodium.* Respiration was controlled by insufflation of 100 per cent oxygen through an endotracheal tube. The animals were cooled to 33° C. in an ice bath. After they were removed from the bath, the esophageal temperature usually stabilized around 30° C. (28° to 32° C.).

A right thoracotomy was carried out through the fourth intercostal space. A large plastic tube was inserted into the right atrium for the gravity drainage of venous blood to the pump-oxygenator. The left femoral artery was cannulated for arterial inflow from the pump and the right femoral artery for monitoring of arterial blood pressure with a mercury manometer. A Sigmamotor pump and a large bubble oxygenator were used. The pump-oxygenator was primed with blood taken from donor dogs anesthetized lightly with methohexital sodium. Total cardiac bypass was established, usually at a flow rate of 40 c.c. per kilogram per minute. The heart was arrested with acetylcholine which was injected into the proximal aorta at a dosage of 10 mg. per kilogram of body

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weight. The left atrium was entered through the interatrial groove. The atrium was completely cleared of blood by an aspirator. In one group of animals, the central and basal portion of the aortic leaflet of the mitral valve was then incised close to and essentially parallel to the annulus. An elliptical piece of tissue, about 1 by 0.5 cm. in size, was excised. The defect was then grafted with a slightly larger piece of nylon or Teflon cloth. This was sutured into place with two or three running sutures of 5-0 arterial silk (Fig. 1, *a*).

In another group, the septal leaflet and attached chordae tendineae were excised but for a small rim of leaflet tissue next to the annulus. An artificial leaflet was then fashioned from synthetic fabric. The outline was similar to that of the normal leaflet. It was sutured above to the rim of leaflet tissue adjacent to the annulus, and below two extensions were sutured to each papillary muscle (Fig. 2, *a*). The left atrium and ventricle were then filled with saline solution and the left atrial wall was closed. The aspiration of the proximal aorta was carried out with a small needle before the aortic occlusive clamp was removed. In many instances, air was present in this location. If ventricular fibrillation occurred, it was converted to a more normal rhythm with electrical shock.

Total cardiopulmonary bypass time ranged from 30 to 50 minutes and cardiac arrest from 20 to 40 minutes. The animals were re-warmed by immersion in hot water at 42° C. until the esophageal temperature reached 35° C.

EXPERIMENTAL RESULTS

Initially, operations were done without sterile precautions. Many animals did not survive because of errors in surgical technique or in the management of the cardiopulmonary bypass. Air embolism was a particularly difficult problem. Some survived the initial postoperative period only to die from 3 to 7 days afterward from partial or total dehiscence of the suture line of the graft. Some failures resulted from infection and septic thrombosis of the left atrium; other failures were a result of suturing the plastic material to an area of the leaflet which was too thin and delicate. Dehiscences of the suture line were characteristically located near the free edge of the leaflet where the valve substance was thinnest (Fig. 1, *b*). These animals would characteristically do well for 1 to 3 days after the operation; they would then suddenly become ill and die within a few hours.

As a result of these experiences, the operative technique was altered so that the incision in the leaflet was located in the thicker, more basal portion close to the annulus. Separation of the suture line did not then occur. Five animals, operated upon under aseptic conditions, tolerated partial replacement of the major leaflet well and lived an active kennel life until the time of sacrifice. No cardiac murmurs were heard. In 3 of the 5, the left atrial and left ventricular pressures were taken 3 months after the grafting procedure. The pressure tracings were entirely normal and showed no evidence of mitral insufficiency. In 4, nylon cloth was interpolated into the valvular defect, and in the fifth, Teflon was used. The animals were sacrificed 3 months after the operative procedure. All of the grafts were invested with a layer of fibrous tissue which had

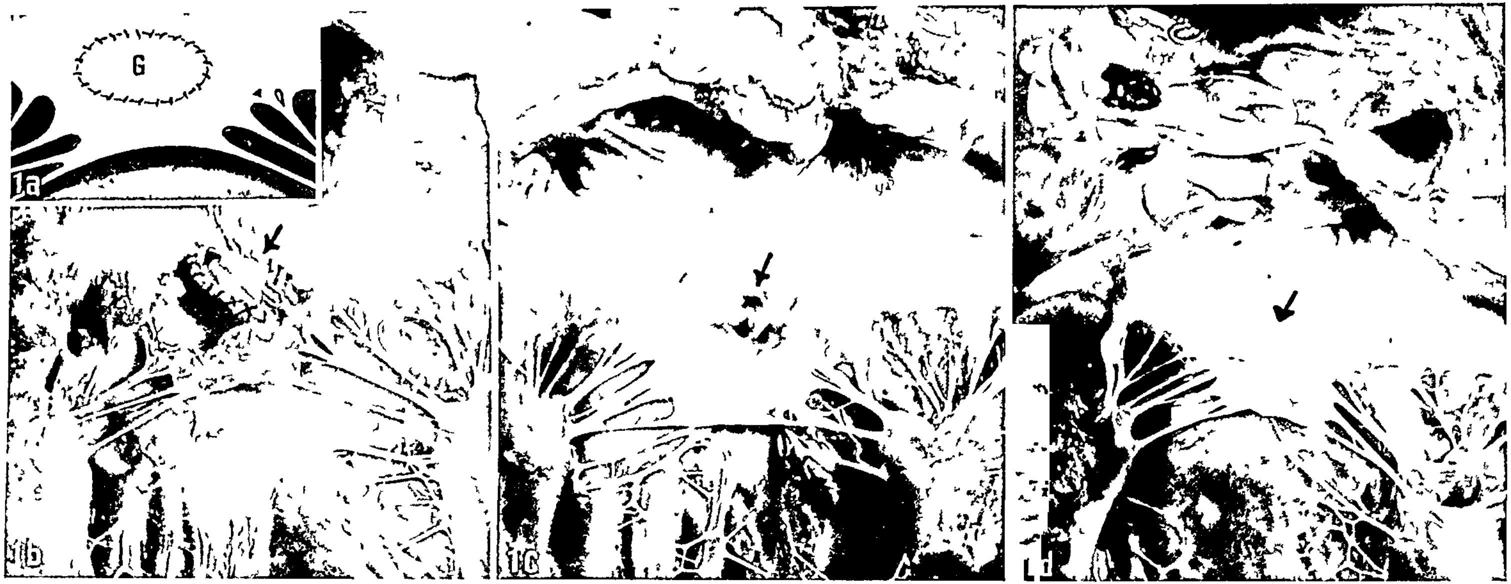

Fig 1 —A group of illustrations showing the major leaflet of the mitral valve partially replaced with a graft of synthetic fabric

a A drawing which shows the usual position and form of the graft

b A photograph which shows partial dehiscence of the medial part of the suture line The sutures remain attached to the graft This animal made an excellent recovery until the third day after operation when it suddenly became ill and died from mitral regurgitation

c, A photograph of the major mitral leaflet of an animal which was sacrificed 3 months after operation The graft was made of nylon The arrow points to a raised area near the center of the graft which was composed of an overgrowth of fibrous tissue

d, A photograph of the major mitral leaflet of an animal which was sacrificed 3 months after operation The arrow points to the graft. It was made of Teflon The fabric is covered with a thin smooth layer of fibrous tissue a smooth endothelial-like surface. One showed a moderate amount of fibrous thickening in the region of the suture line (Fig. 1, *c*). In the others, the plastic cloth was covered with a very thin layer of fibrous tissue (Fig. 1, *d*). None demonstrated any significant contracture of the leaflet tissue itself.

Complete replacement of the major leaflet was carried out on 5 animals with aseptic precautions Nylon cloth was used in 2. One lived 10 and the other 13 days. Both died in congestive heart failure. Autopsy revealed mitral insufficiency to be present at both extremities of the graft. It was our impression that the valve function could be improved by increasing the area of the synthetic leaflet. Teflon cloth was used in the next 3 dogs The grafts were made larger in size. One animal survived 18 days Death resulted from dehiscence of the thoracotomy incision. Autopsy showed the valve to be competent Another did well for 5 days and then died suddenly. Autopsy revealed one limb of the graft had become detached from the papillary muscle Severe overwhelming mitral insufficiency resulted (Fig 2, *b*). The third dog did well for about 6 weeks when it became sick and inactive. The animal was sacrificed at 7 weeks. Once again the graft was found to be separated from one of the papillary muscles.

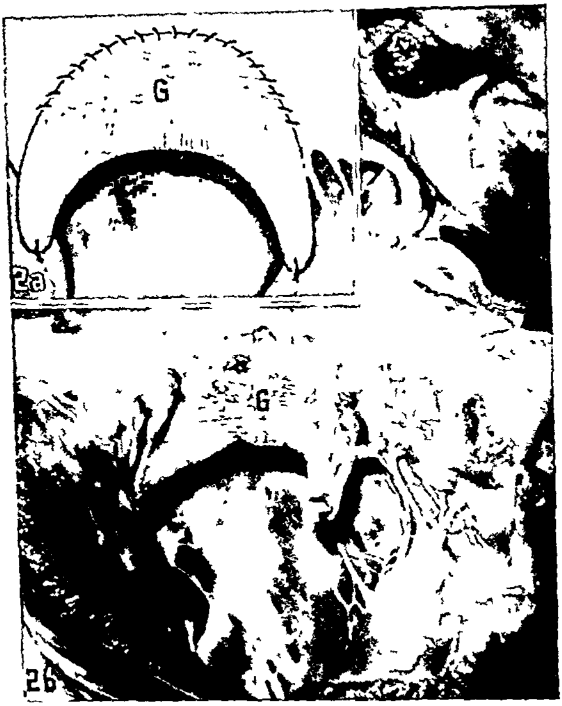

Fig 2.—Two illustrations showing complete replacement of the major leaflet and attached chordae tendineae with synthetic fabric

a, A drawing which shows the size and configuration of the artificial leaflet. The two lateral extensions of the graft were sutured to the papillary muscles The extensions prevented eversion of the graft

b, A photograph of an artificial leaflet of Teflon fabric Following placement of the graft the animal remained in good health for 3 days and then became sick and died Overwhelming mitral insufficiency resulted when a lateral extension of the graft became detached from a papillary muscle The suture remained attached to the graft The fabric is partially covered with a smooth layer of fibrin

Neither of the synthetic fabrics used in this experiment was entirely suitable for valve replacement. Sutures frequently pulled out of the nylon cloth even though the edge was carefully coagulated with heat. The nylon was thin and approximated the consistency of the leaflet tissue; however, it was inelastic and had a tendency to wrinkle. Sutures held well in the woven Teflon without special treatment of the cut edge. Unfortunately, the Teflon fabric which was commercially available was considerably greater in thickness and much less flexible than the mitral leaflet of the dog. Both fabrics were difficult to work with because of their inelasticity and relative inflexibility. Theoretically, the changing size of the mitral annulus and the normal variation in curvature of the leaflet from concave to convex with each heartbeat would make permanent pliability of the graft material most desirable. For replacement of a large area or a complete leaflet, elastic fabrics and living homologous tissues, such as atrial wall, should be investigated. The commercially available woven Teflon fabric should be satisfactory in most instances for partial leaflet replacement in patients.

Our results demonstrated that synthetic fabrics could be used successfully for partial replacement of the major leaflet of the mitral valve. The diaphanous character of the mitral leaflet of the dog made the technical problem of suturing the graft to the leaflet a difficult one. Good healing could not be expected if a portion of the suture line was located in the extremely thin medial area. When the graft was placed in the thicker basal part of the valve, better results were obtained.

Attempts to replace completely the major leaflet of the mitral valve were all eventually unsuccessful. The synthetic leaflets were made similar in configuration but slightly larger than normal. These functioned astonishingly well for short periods of time. Dehiscence of the attachment of an extension of the graft to a papillary muscle was the most common cause of failure. This fault undoubtedly could be corrected by a change in operative technique. Fabrics more suitable for valve replacement than those used in this study should also improve the results. Whether the flexibility of the graft would ultimately be lost as the fabric became covered with fibrous tissue was a question this study did not resolve. In the 1 animal that survived 7 weeks following complete replacement of the major leaflet, the fabric was relatively stiff at the time of autopsy. In view of the excellent functional results obtained in the early postoperative period, it would appear reasonable that complete leaflet replacement would be feasible once suitable replacement fabrics or tissues are found.

SUMMARY

1. Synthetic fabrics can be used successfully for partial replacement of the major leaflet of the mitral valve.

2. The problem of complete leaflet replacement is a difficult one and should be studied further. Some animals had good function of the mitral valve for short periods of time. All, however, eventually died from mitral insufficiency.

THE EVALUATION OF MITRAL STENOSIS WITH SELECTIVE LEFT VENTRICULAR ANGIOCARDIOGRAPHY

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Left ventricular angiocardiography is never primarily indicated for the evaluation of the stenotic component in mitral valvular disease. Introduction of contrast medium direct into the left atrium by percutaneous injection over the ninth rib paravertebrally on the right side will provide much more reliable information about a mitral stenosis when this is needed. In the course of left ventricular angiocardiography in the evaluation of mitral insufficiency and aortic stenosis we have observed a typical doming of the stenosed mitral valve. After correlation of this roentgenologic sign with the findings at surgery, we consider it to be of significant diagnostic value.

METHOD

The patient is examined in the supine position, a needle being introduced through the apex beat and directed toward the second right costochondral junction. The procedure is performed under local anesthesia. One to one and one-half milliliters of 76 per cent Urografin per kilogram of body weight is injected at a rate of 30 ml. per second. The exposures (maximum time, 0.03 sec.) are made in two planes (frontal and lateral projection) with a frequency of 6 frames per second during and 1 to 2 seconds after the injection. The examination is concluded with a series of frames taken at a frequency of 1 to 2 per second. During and 1 to 2 seconds after the injection, the carotid arteries are compressed in order to reduce the flow of contrast medium to the brain.

RESULTS

1. *Open Mitral Orifice.*—No dome formation was found in cases in which there was no mitral stenosis. One patient with a normal heart was investigated (Fig 1, *A* and *B*). In this case the blood from the left atrium during diastole rapidly found its way into the left ventricle causing a filling defect in the valvular area. In the anterior projection, however, the defect was sharply outlined in its inferior part only, and not all around, as will be demonstrated in the cases with typical doming of the fused mitral valves. In most patients with no mitral stenosis, the anterior projection will show at most a poorly defined defect in the ventricular contrast (Fig. 2, *A*).

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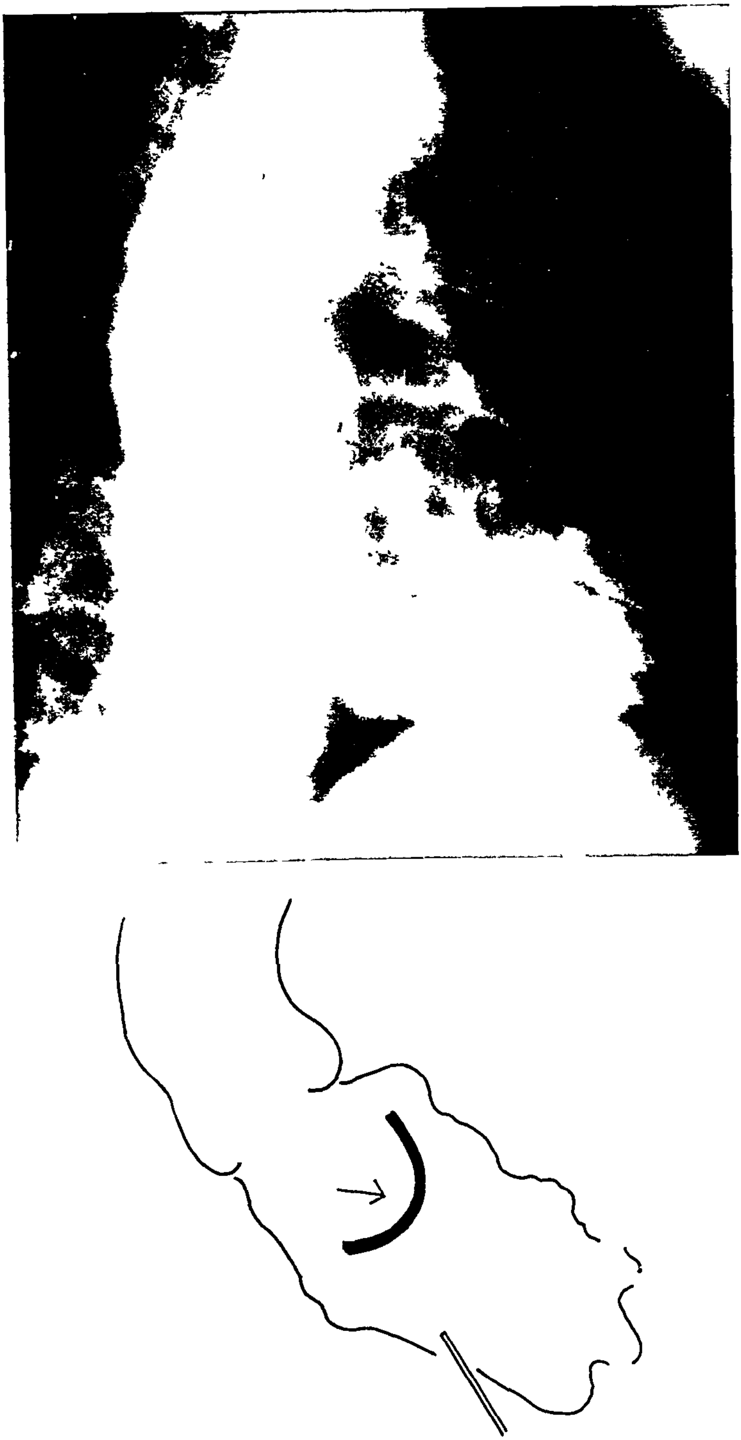

Fig 1 — A 42-year-old man with a normal heart and a malignant tumor of the thymus Left ventricular angiocardiograms in ventricular diastole *A*, Frontal projection In the upper part of the left ventricle a filling defect the size of a walnut, with a sharp inferior border (→)

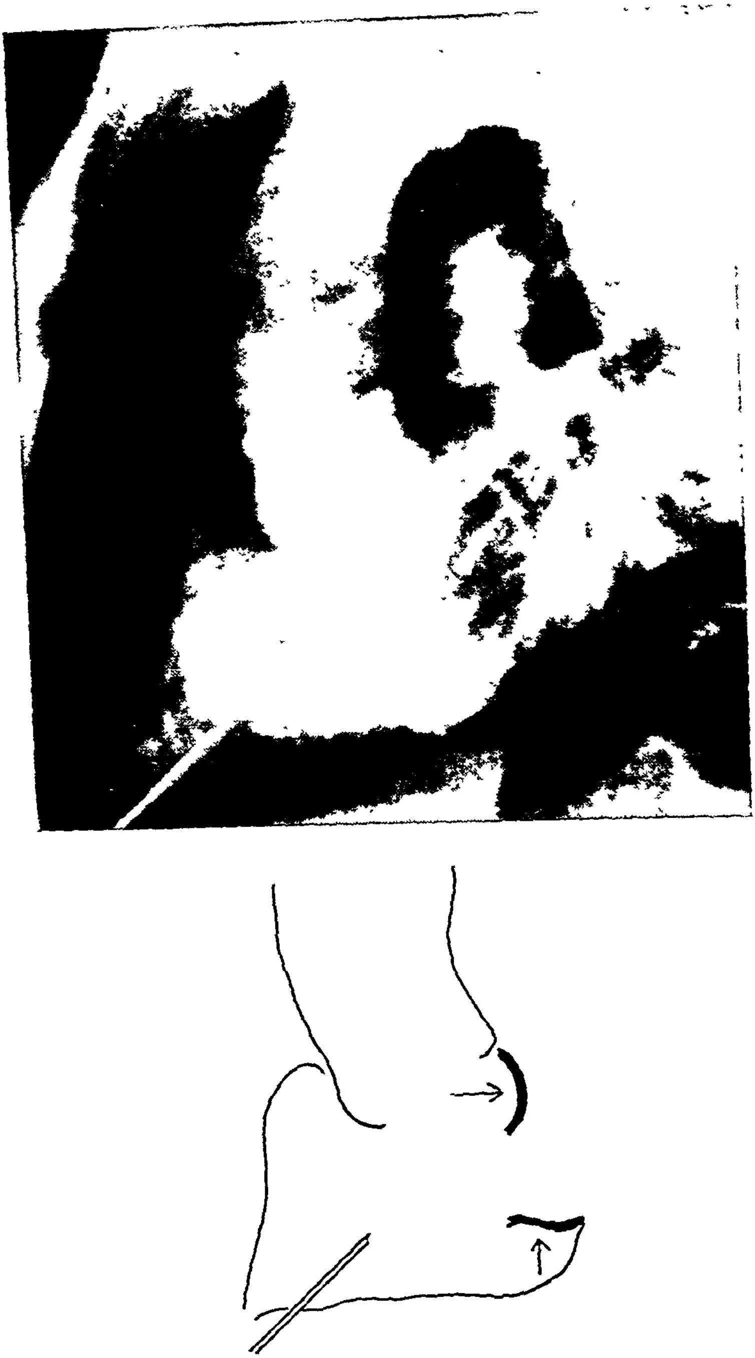

Fig. 1.—*Cont'd.* *B*, Lateral projection. The mitral leaflets are partly visualized. The posterior leaflet (↑) is more or less parallel to the x-ray beam and is therefore responsible for the sharp inferior border of the defect in the anterior projection. The anterior leaflet (→), however, is oblique to the x-ray beam and is not distinctly outlined in the anterior projection. The area between the leaflets has a poorly defined anterior border, caused by the rapid mixing of the contrast medium with blood from the left atrium. No doming.

In cases of a patent mitral orifice, the leaflets may be seen in the lateral projection during diastole (Figs. 1, *B* and 2, *B*). The valvular area is not sharply outlined anteriorly, owing to the rapid emptying of the left atrium and immediate dilution of the contrast medium in the left ventricle; thus, no dome is visible.

2. *Mitral Stenosis.*—When the mitral valves are fused to form a dome during diastole, this dome will bulge into the left ventricle making a sharply outlined filling defect in the left ventricle. This formation is seen in both the frontal and lateral projections (Figs. 3, *A* and *B*, and 4, *A* and *B*). In all 20 patients operated upon, in which a dome had been found preoperatively in the left ventricular angiocardiogram, mitral stenosis was found at operation. The stenosis was severe in all but 1 case in which it was very mild, admitting 1½ fingers.

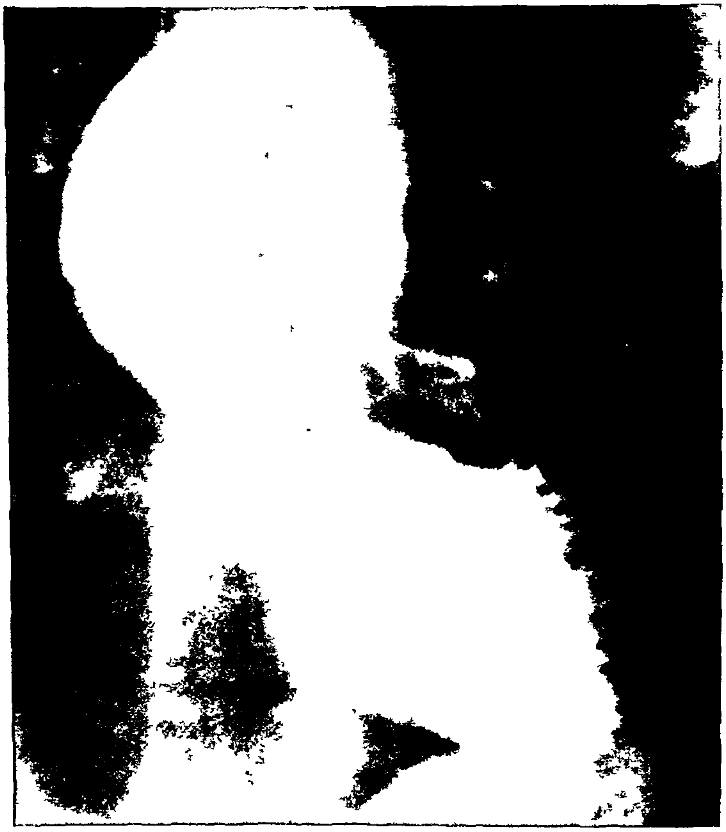

Fig. 2.—A 27-year-old man with pure aortic stenosis. Left ventricular pressure was 164/20 mm Hg. Pressure gradient over the aortic valves was 27 mm Hg. Pulmonary capillary pressure was 9 mm. Hg. Pulmonary artery pressure was 20 mm Hg. Left ventricular angiocardiograms in ventricular diastole. *A*, Frontal projection. In the mitral valvular area of the left ventricle a small, poorly defined, filling defect can be seen, caused by the inflow of blood from the left atrium.

In cases of combined mitral stenosis and mitral insufficiency, it may be difficult to demonstrate doming if the insufficiency is severe, since contrast medium then becomes mixed with blood in the left atrium and no distinct

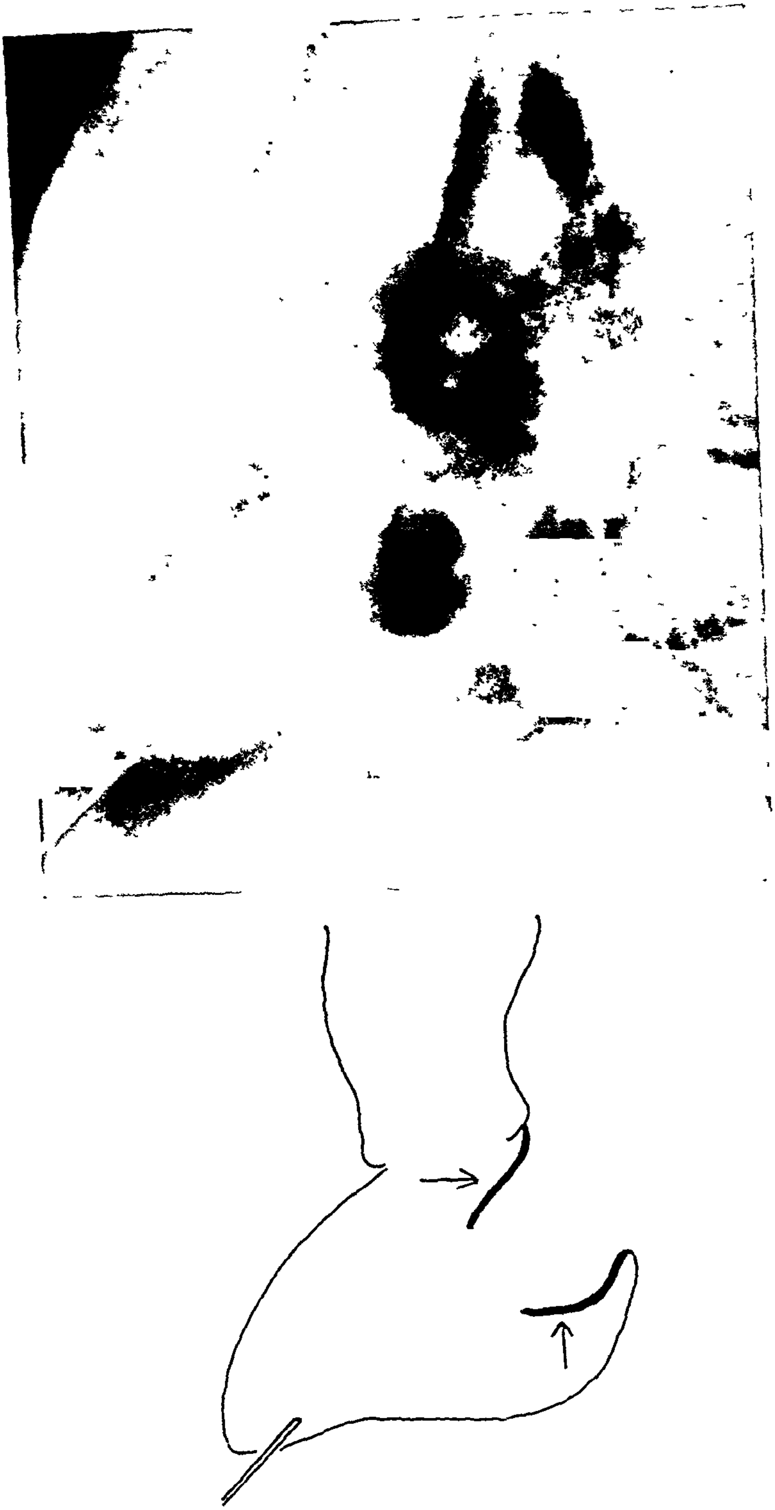

Fig. 2.—Cont'd. *B*, Lateral projection. The open mitral orifice is seen and the mitral leaflets are partly visualized. Rapid mixing of the blood from the left atrium and the contrast medium between the leaflets causes an anterior border that is not sharp. No doming. Anterior (→) and posterior (↑) mitral leaflet.

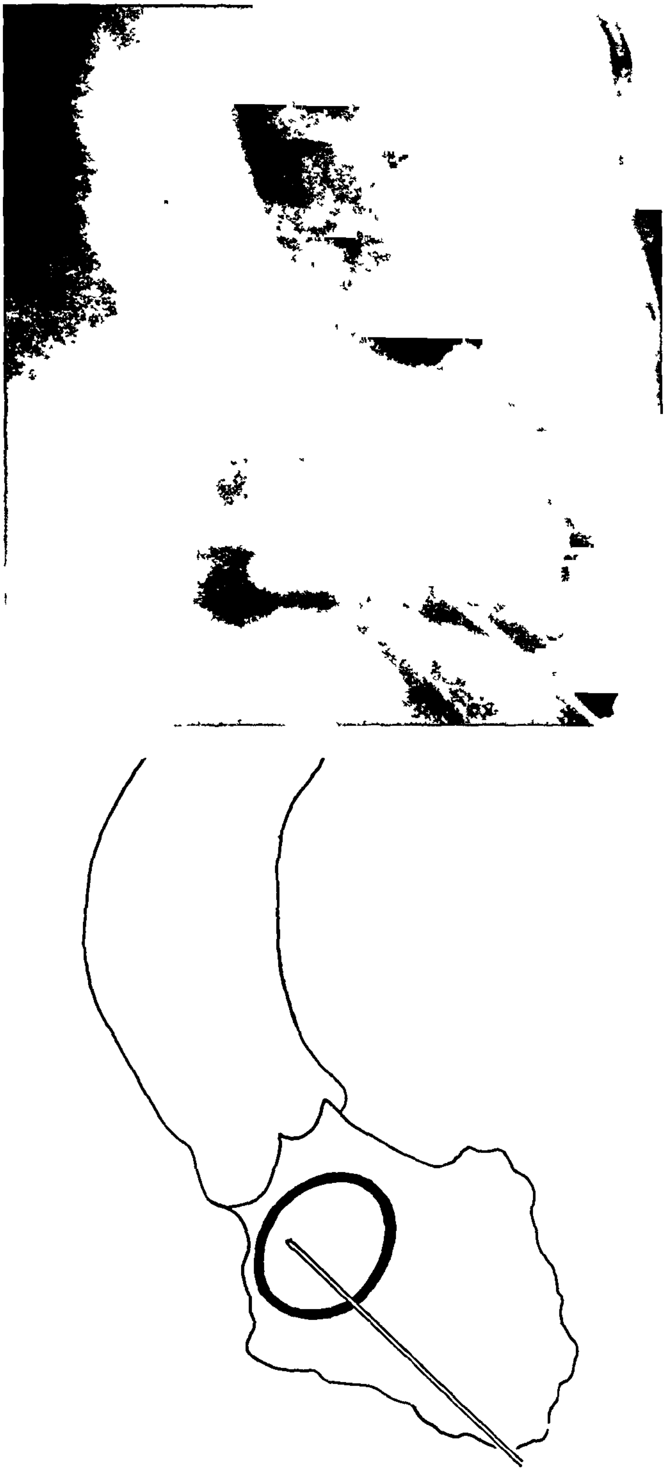

Fig 3—A 49-year-old woman with mitral and aortic stenosis (no pressure gradient over the aortic valves) and mitral insufficiency At operation there was a rigid mitral stenosis with an opening, 10 mm long Transventricular dilatation of both mitral and aortic stenosis Left ventricular angiocardiograms i
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the aortic orifice an oval, clearly
filling defect is seen The defect is
caused by the fused mitral leaflets
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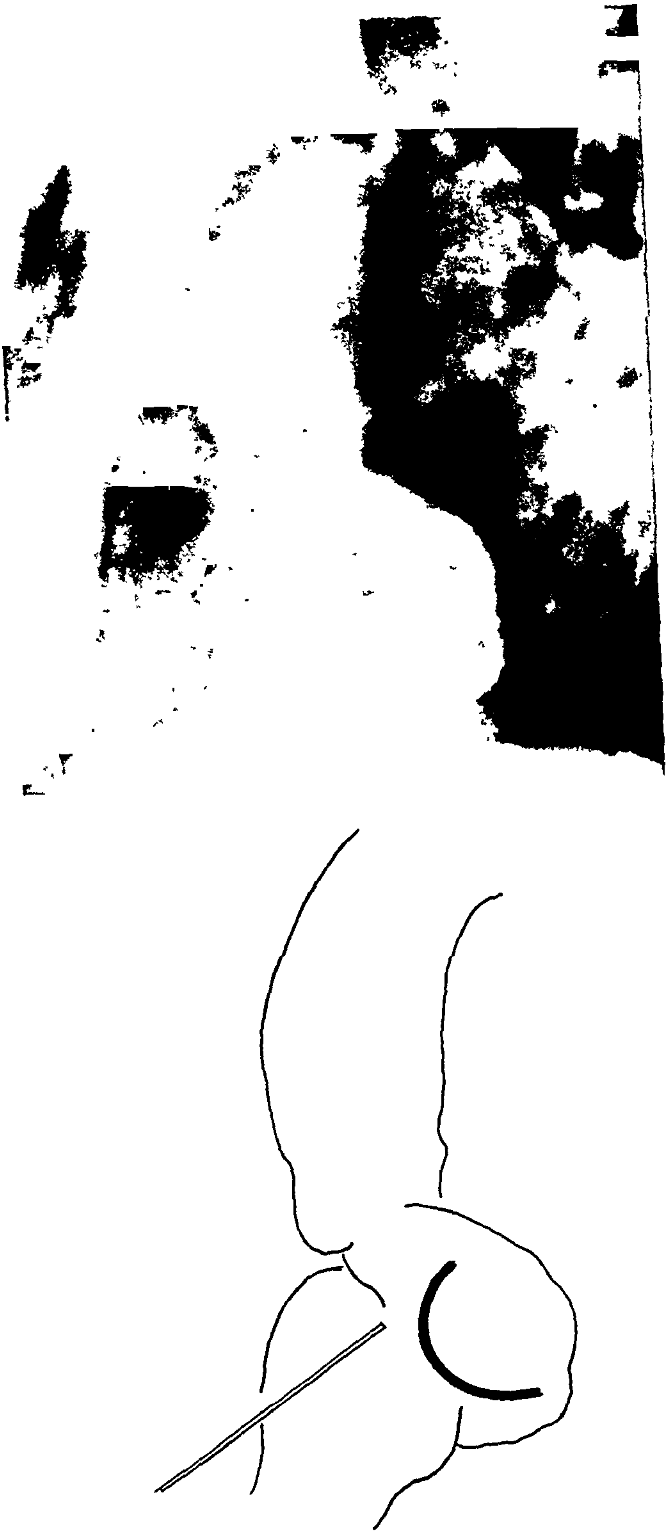


Fig. 3.—Cont'd. *B*, Lateral projection. The fused mitral leaflets form a sharply outlined dome bulging into the ventricle.

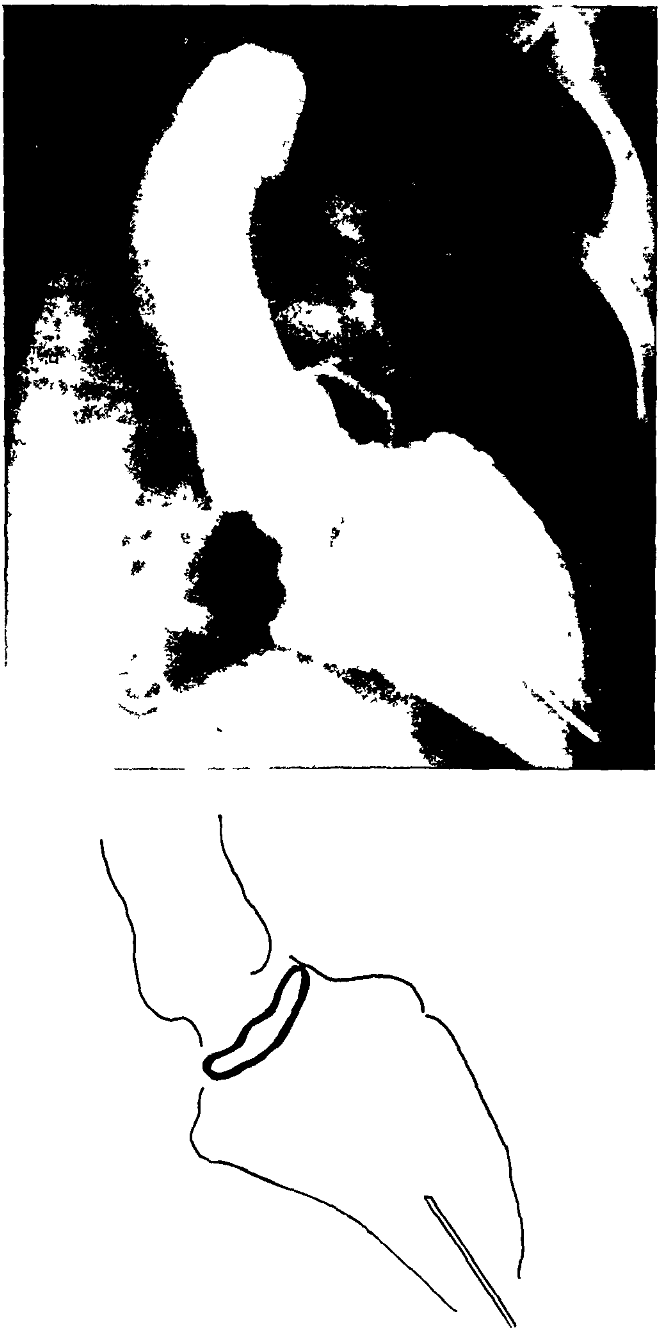


Fig. 4.—A 42-year-old woman with mitral re-stenosis. At reoperation, the mitral orifice was found to admit the tip of the little finger. Pulmonary artery pressure was 15 mm Hg; pulmonary capillary pressure (systolic) was 30 mm Hg—during work it was 57 mm Hg. Left ventricular angiocardiograms in diastole. *A*, Frontal projection. Slit-like, sharply contoured defect in the mitral valvular area. In this case the inferior border is caused by the anterior leaflet and the superior border of the posterior leaflet.

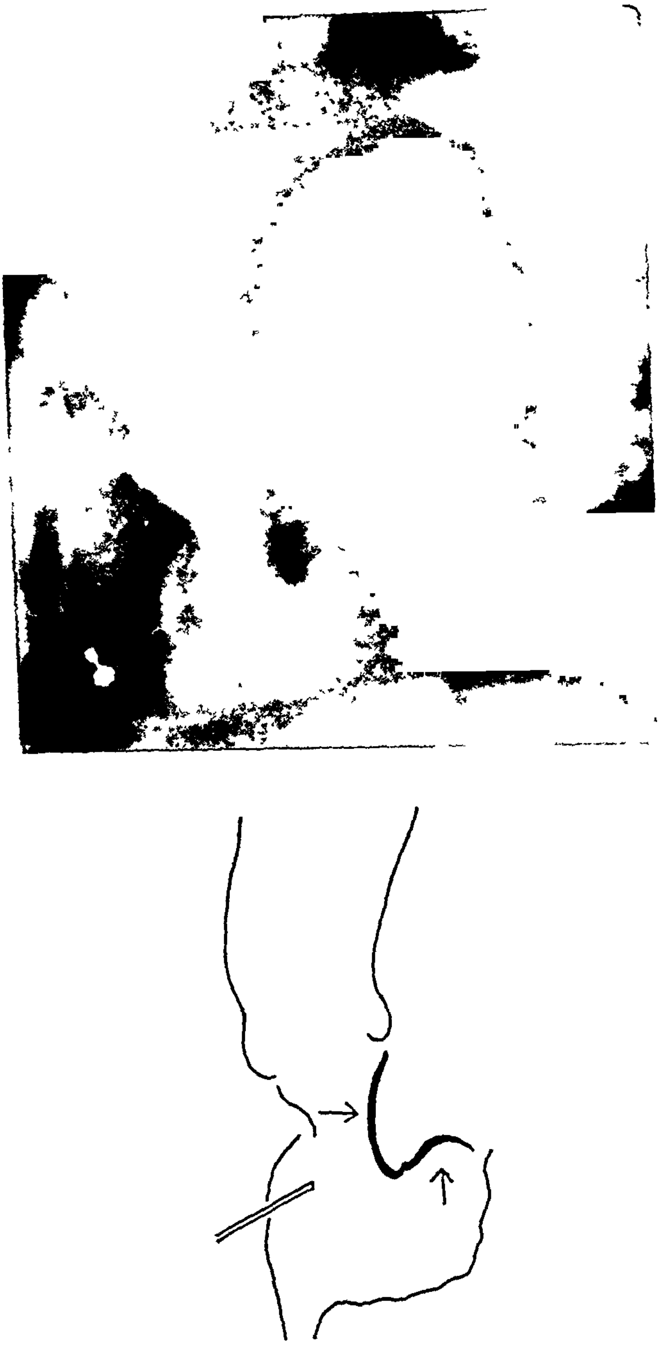
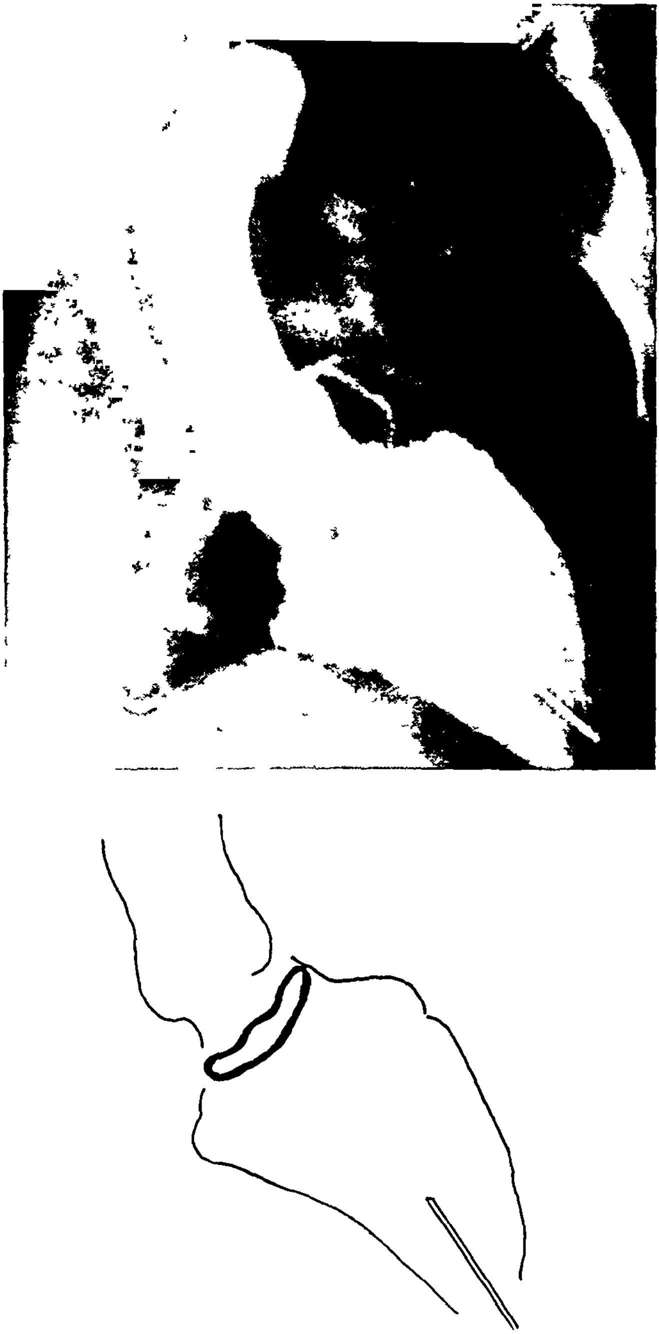


Fig. 4.—Cont'd. *B*, Lateral projection. The anterior leaflet (→) bulges forward, and its border is pulled down. The posterior leaflet (↑) is thickened, and its upper border is projected above the border of the anterior leaflet.



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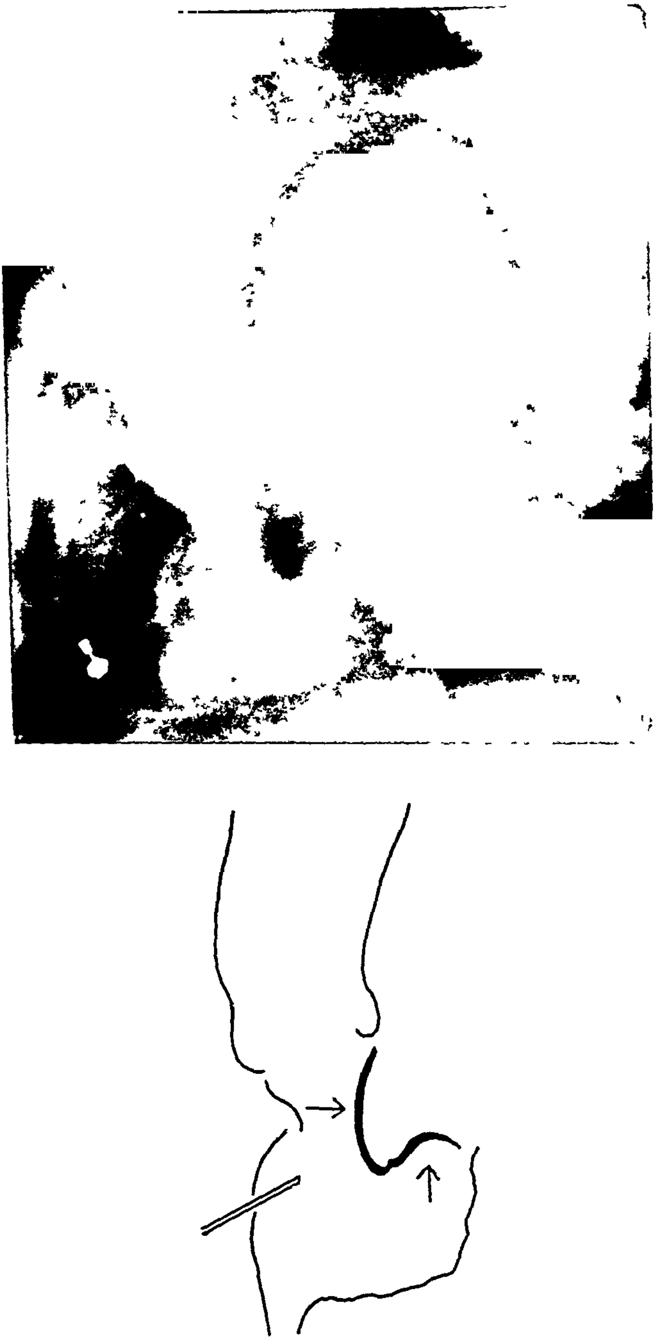

Fig. 4.—Cont'd *B*, Lateral projection. The anterior leaflet (→) bulges forward, and its border is pulled down. The posterior leaflet (↑) is thickened, and its upper border is projected above the border of the anterior leaflet.

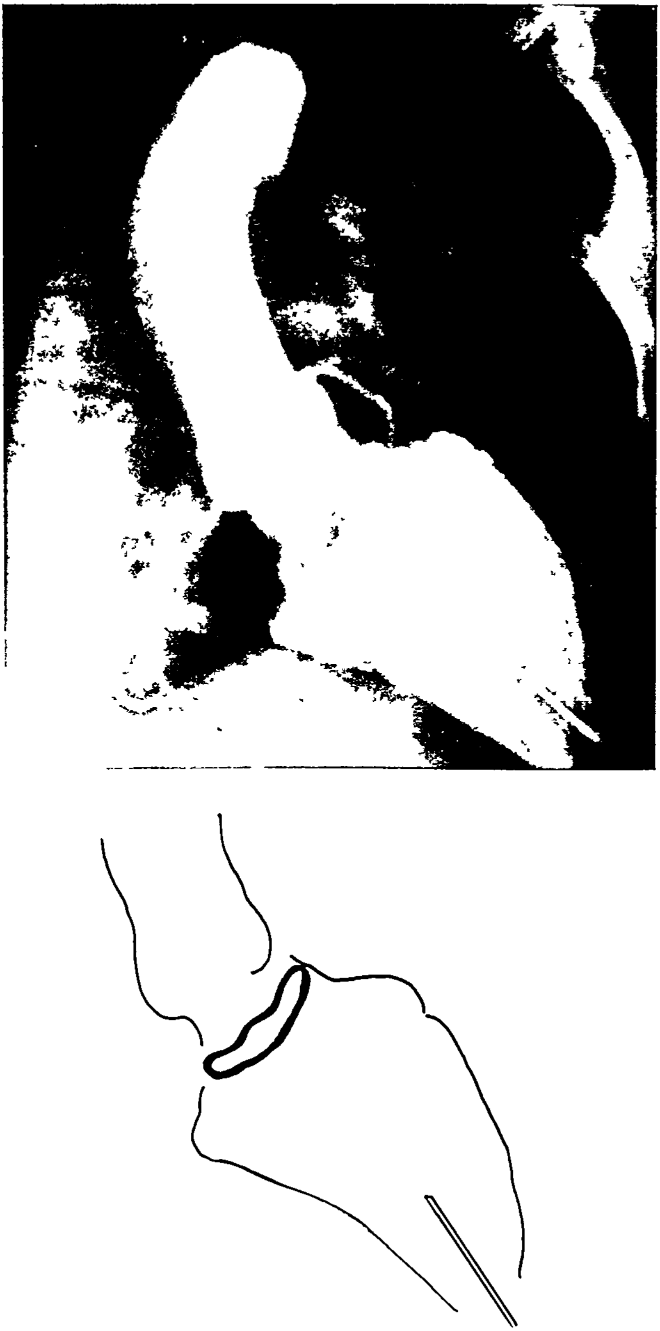

Fig. 4—A 42-year-old woman with mitral re-stenosis At reoperation, the mitral orifice was found to admit the tip of the little finger Pulmonary artery pressure was 15 mm. Hg, pulmonary capillary pressure (systolic) was 30 mm. Hg—during work it was 57 mm. Hg. Left ventricular angiocardiograms in diastole A, Frontal projection Slit-like, sharply contoured defect in the mitral valvular area. In this case the inferior border is caused by the anterior leaflet and the superior border of the posterior leaflet.

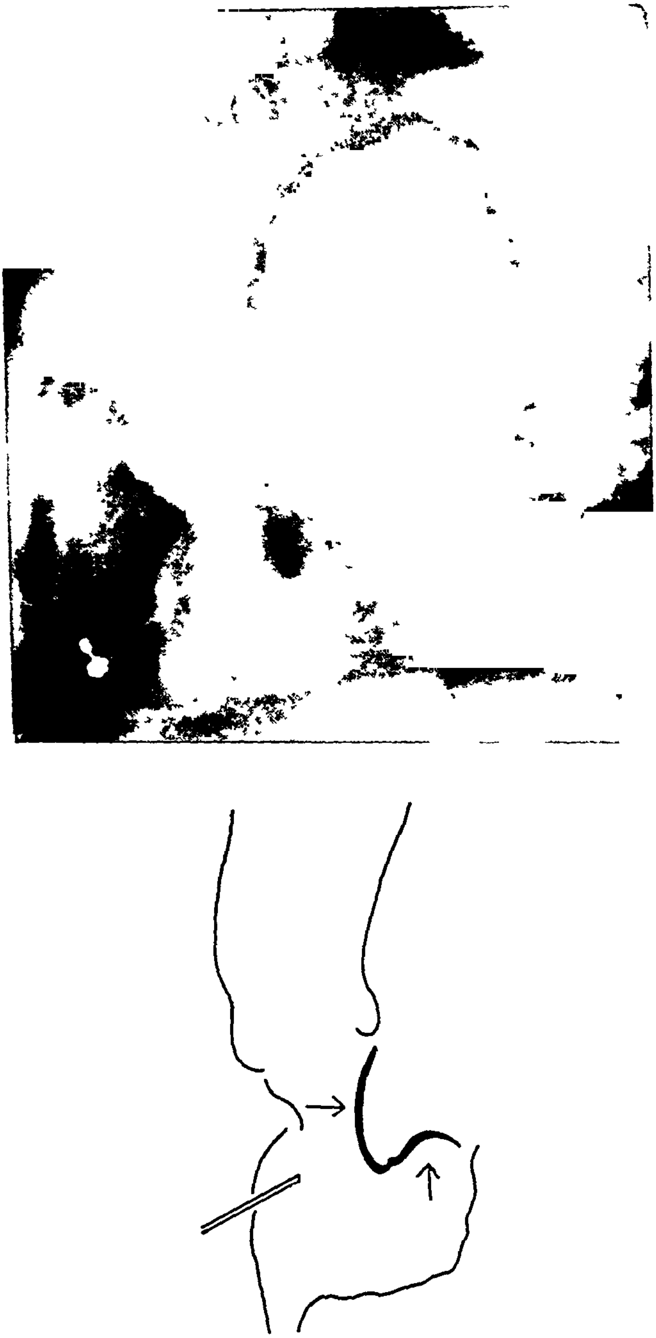

Fig 4.—Cont'd *B*, Lateral projection. The anterior leaflet (→) bulges forward, and its border is pulled down. The posterior leaflet (↑) is thickened, and its upper border is projected above the border of the anterior leaflet.

difference between atrial and ventricular contrast density can be made out. In these cases the dome will only be outlined at the beginning or the end of the cycle.

3. *The False Dome.*—It is most important to see the doming of the mitral valves in both anterior and lateral views to establish the diagnosis of mitral stenosis. In the lateral projection the atrial wall may simulate a dome caused by fused mitral valves, but in such cases no dome can be seen in the anteroposterior projection. Furthermore, this false dome in the lateral projection will persist during systole (Fig. 5, *A-D*).

Fig. 5.—A 31-year-old woman with pure mitral insufficiency. Exploratory cardiotomy revealed a severely incompetent mitral orifice admitting 2 fingers. Left ventricular angiocardiograms. *A*, *Frontal projection*. Diastole. No ventricular filling defect.

CONCLUSION

Ordinarily the inferior border of the filling defect seen in the anterior projection may be sharply outlined and caused by the mitral annulus itself, the short posterior mitral leaflet lying tangential to the x-ray beams in diastole (Fig. 1). Usually the superior border is not distinctly outlined since, in diastole, the anterior mitral leaflet is projected obliquely to the plane. Furthermore, the rapid emptying causes immediate dilution of the contrast medium resulting in a poorly defined border between this and blood. A diagnosis of mitral stenosis can only be accepted if, (1) the contrast defect is observed in both planes, and (2) the defect in the anterior plane is sharply outlined all

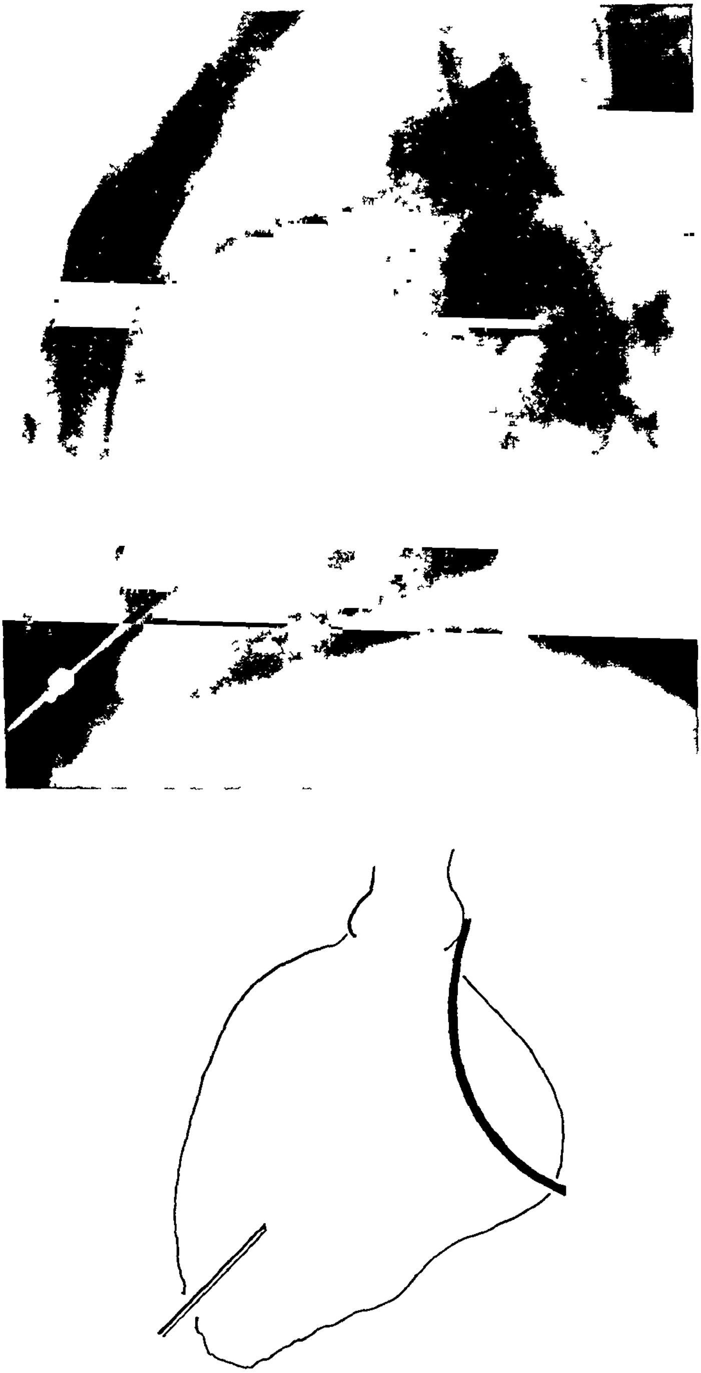

Fig 5 —Cont'd *B, Lateral projection* Diastole Dome formation resembling true mitral doming

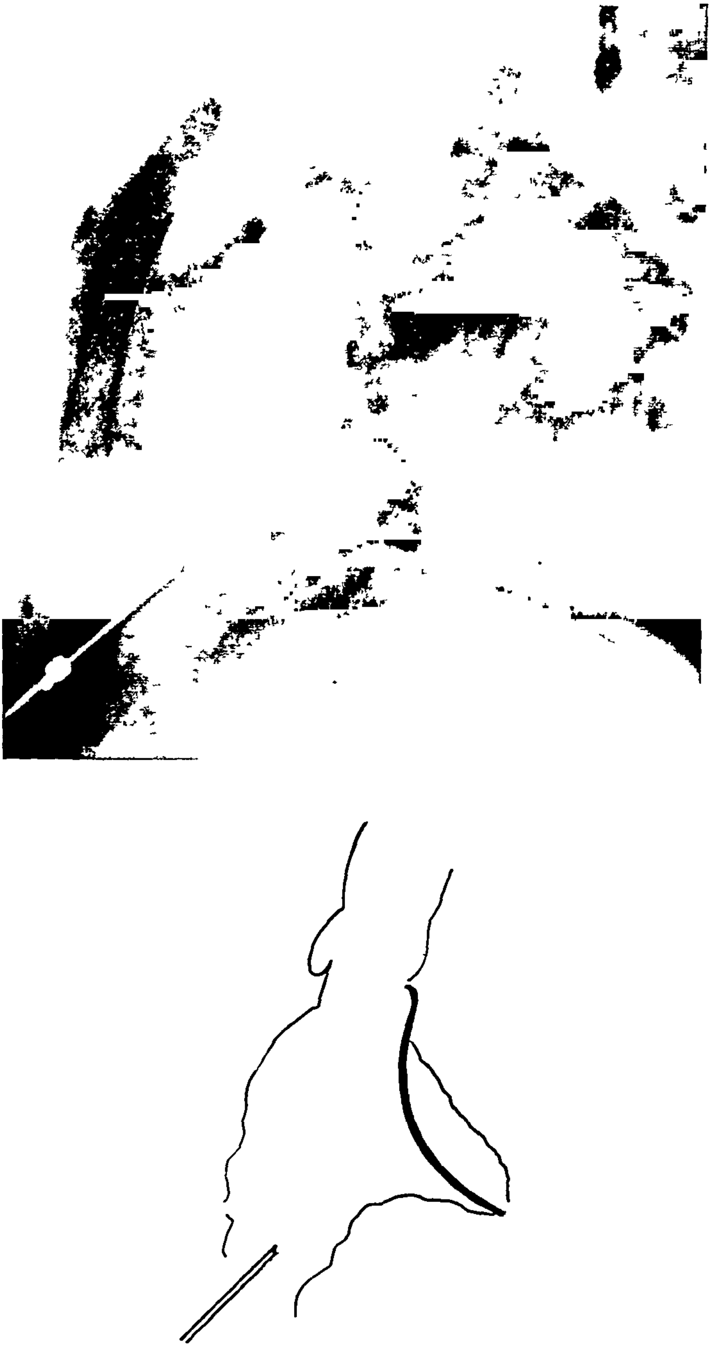

Fig. 5.—Cont'd. *C*, Systole. The dome formation is unchanged.

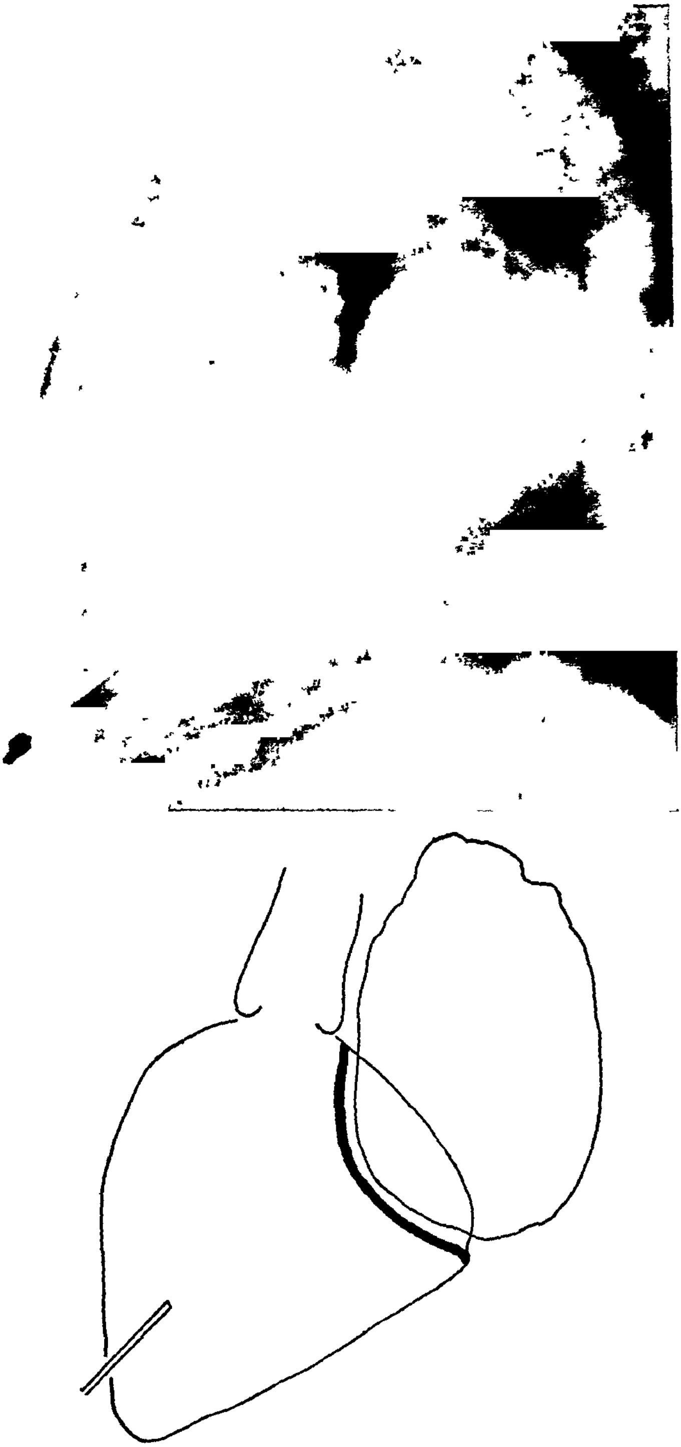

Fig. 5.—Cont'd *D*, Diastole The left atrium filled with contrast medium. The dome formation corresponds to the atrial wall.

around. This is due to the slow emptying of blood from the left atrium and the forward bulging of the fused mitral valves. The doming will cause one part of the anterior leaflet to lie parallel to the x-ray beams and therefore to be visualized. Thus, the anterior mitral leaflet will act as a bulging sail behind which a pool of contrast-free blood projects into the left ventricle (Fig. 6).

In most cases the filling defect has been rounded, but owing to the relation between an eccentric orifice and the projection used, the defect may appear more slit-like and the border of the anterior leaflet may sometimes even be viewed below that of the posterior leaflet (Fig. 4).

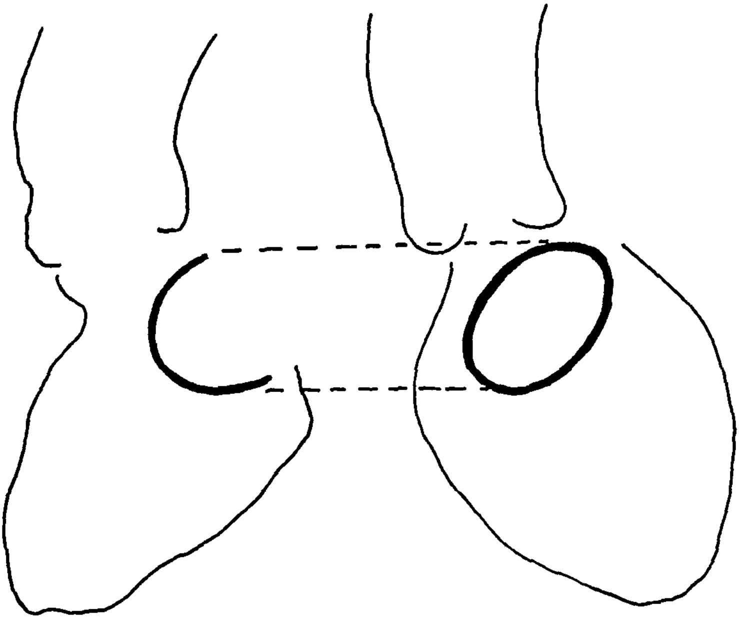

Fig 6.—Diagram which illustrates the visualization of the mitral dome *Left side*—Lateral projection *Right side*—Frontal projection

The absence of a dome in the anterior projection in cases of an enlarged left ventricle cannot exclude the presence of a mitral stenosis, as excessive contrast medium in the left ventricle will mask the dome.

SUMMARY

During a series of selective left ventricular angiograms, we have observed a clearly visible and sharply outlined filling defect in the left ventricle caused by the fused mitral valves forming a dome and projecting down into the left ventricle. When this dome is visible, sharply outlined in both lateral and anteroposterior projections, it constitutes evidence for the diagnosis of mitral stenosis. It must be distinguished from the left atrial wall, which will be seen projecting into the left ventricle only in the lateral projection.

The roentgenologic diagnosis has been confirmed at operation.

TRICUSPID ATRESIA

Treatment by Superior Vena Cava–Pulmonary Artery Anastomosis

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After much animal experimentation,[1-4] Glenn reported the clinical application of a superior vena cava to pulmonary artery anastomosis. This unique anastomosis has had a longer and more extensive trial in Russia[5] and in some centers is favored over the Blalock or Potts types of anastomosis for cyanotic congenital heart disease. Tricuspid atresia is one anomaly not yet amenable to open-heart surgery and in the following case such gratifying results were obtained by a superior vena cava to pulmonary artery anastomosis that it would seem that further attention should be drawn to this procedure.

CASE REPORT

T. H., a girl, was born 3 weeks prematurely. Pregnancy, delivery, and neonatal course were uneventful. A cardiac murmur was noted at age 3 days. At the age of 6 weeks, the infant was doing well, no cyanosis was noted, but the murmur was still present. At 7 weeks of age, following a mild gastrointestinal upset, cyanosis developed suddenly, and the infant was in severe distress. On admission to the hospital, cyanosis was severe, pulse was 200, liver edge was 3 cm. below the costal margin, and a Grade 3 systolic murmur was heard along the left sternal border. Severe cyanosis persisted despite oxygen therapy and digitalis, and two anoxic attacks were observed.

X-ray studies of the chest showed moderate cardiac enlargement, a concave pulmonary artery segment, decreased lung vascularity, and a pneumonic area in the right middle lobe. The electrocardiogram showed left axis deviation (minus 30 degrees) and a clinical diagnosis of tricuspid atresia was made. An angiocardiogram, with a catheter high in the inferior vena cava, showed (Fig. 1) the atresia of the tricuspid valve and a small patent foramen ovale. Additional films (Fig. 2) showed this to be a type 1b of Keith and associates[6] with a small ventricular septal defect, a rudimentary right ventricle, and a small pulmonary artery. The aortic arch was on the right side.

Using the operative technique of Glenn,[4] the right pulmonary artery was anastomosed to the superior vena cava and the junction of the latter to the right atrium was occluded (Fig. 3). The entire operative procedure lasted less than one hour.

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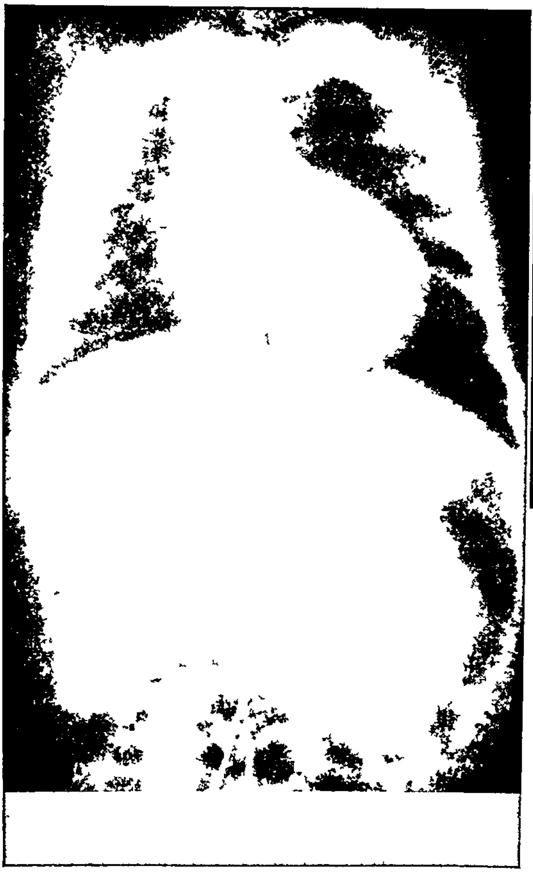

Fig 1

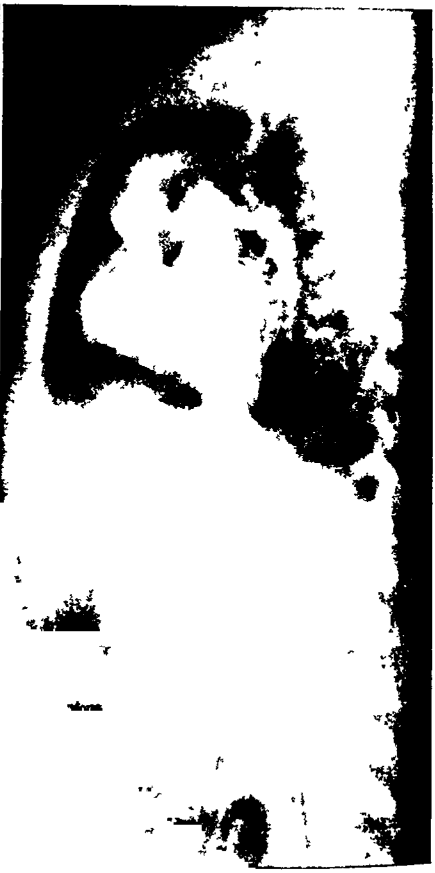

Fig 2

Fig 1—An angiocardiogram posteroanterior view, which shows atresia at the tricuspid valve area, and a jet of medium traversing a patent foramen ovale

Fig 2—Later film, lateral view, which shows the rudimentary right ventricle and small pulmonary artery

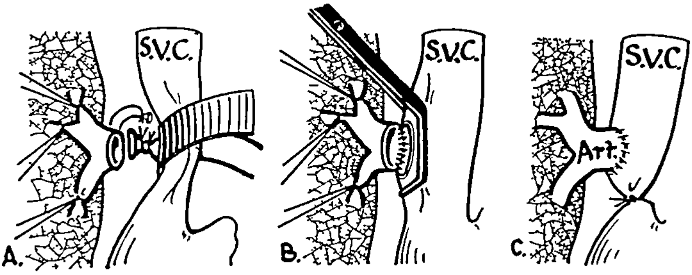

Fig 3—Operative procedure *A*, Ligation of the proximal end of the right pulmonary artery *B*, End-to-side anastomosis of the pulmonary artery to the superior vena cava. *C*, Ligation at the superior vena cava right atrial junction

An immediate postoperative improvement in the cyanosis was noted, although for the first 4 postoperative days moderate puffiness and cyanosis of the face, neck, and arms was noted. The infant was discharged 12 days after operation. When seen at age 5 months, 14 weeks after surgery, the infant continued to do well. The weight was 5.6 kilograms compared to a birthweight of 2.5 kilograms and a weight at 7 weeks of 3.3 kilograms. Heart size showed little change. Auscultatory findings were unchanged and there was no continuous murmur. There was no facial puffiness, although venous pressure in the right arm was 19 mm. Hg. The ear oximeter showed 85 per cent oxygen saturation, bearing out the just detectable clinical cyanosis. Injection of opaque medium into a right antecubital vein showed the anastomatic area and the filling of the right pulmonary artery from the superior vena cava.

DISCUSSION

Early surgery is necessary in tricuspid atresia. Half of all cases fail to survive past 6 months of age.[6] The type reported rarely survives infancy.[7] Pulmonary artery thromboses may occur and preclude successful surgery at a later date.[8] Thus, any surgical procedure for tricuspid atresia must be suitable for the small infant. It would appear that a superior vena cava to pulmonary artery anastomosis is not only suitable for small infants, but is technically a more simple procedure and also has theoretical physiologic advantages over the Blalock and Potts anastomoses in cases of tricuspid atresia.

In a series reported by Neill,[9] only 30 per cent of patients, under one year of age, with tricuspid atresia survived a Blalock procedure. In many cases, while anoxia was corrected, left ventricular failure occurred. In the common type of tricuspid atresia the left ventricle is doing all the work of the heart, and standard aortic to pulmonary artery anastomoses further increase the load on the left ventricle. On the other hand an anastomosis of the superior vena cava to the pulmonary artery corrects anoxia without necessarily increasing the load on the left heart. Glenn and co-workers[3] showed that an anastomosis of the inferior vena cava to the pulmonary artery leads to ascites and chronic morbidity. In man further help may be obtained by full use of gravity to aid blood flow. The patient reported has been maintained in a 30 degree head-up position since surgery. The future course is unknown. Growth of anastomotic sites is a vexing problem but it applies to arterial as well as to venous anastomoses. Collateral venous channels may develop between the superior and inferior caval systems so that progressively less percentage of the blood from the upper part of the body will reach the right lung. Thromboses may occur, perhaps more often than with arterial anastomoses. However, Bakulev and Kolesnikov[5] claimed better long-term results with vena cava–pulmonary artery anastomoses than with Blalock or Potts procedures. In view of the advent of total corrective surgery by cardiopulmonary bypass techniques, this type of anastomosis is probably best reserved for cases such as tricuspid atresia in which total anatomic correction is not yet possible.

SUMMARY

The anastomosis of the superior vena cava to the right pulmonary artery has had extensive laboratory application and is physiologically a good operation

which may be used to bypass the right heart in cases of tricuspid atresia The operation increases pulmonary blood flow without increasing left ventricular work. Technically the operation is simple. A successful application of this procedure in a sick 7-week-old infant with tricuspid atresia is reported and discussed.

ADDENDUM

Since submitting this paper for publication, 3 additional patients with tricuspid atresia have had a superior vena cava to right pulmonary artery anastomosis. Two, aged 5 and 10 months of age, have done well, but in the third patient, aged 8 days, it was not possible to perform a successful anastomosis and death occurred 8 hours after surgery. The patient reported continues to do well.

REFERENCES

1. Glenn, W. L, and Patino, J. F.: Circulatory Bypass of the Right Heart. I, Yale J. Biol & Med 27: 147, 1954.
2. Patino, J. F, Glenn, W. L., Guilfoil, P. H., Hume, M., and Fenn, J. E.: Circulatory Bypass of Right Heart. II, S. Forum 6: 189, 1956.
3. Nuland, S. B., Glenn, W. L. W., and Guilfoil, P. H.: Circulatory Bypass of the Right Heart. III, Surgery 43: 184, 1958
4. Glenn, W. L: Circulatory Bypass of the Right Heart. IV, New England J. Med 259. 117, 1958
5. Bakulev, A. N., and Kolesnikov, S. A.: Anastomosis of Superior Vena Cava and Pulmonary Artery in the Surgical Treatment of Certain Congenital Defects of the Heart, J. THORACIC SURG. 37: 693, 1959.
6. Keith, J. D., Rowe, R. D., and Vlad, P.: Heart Disease in Infancy and Childhood, New York, 1958, The Macmillan Company.
7. Edwards, J. E.: In Pathology of the Heart, edited by S. E. Gould, Springfield, 1953, Charles C Thomas, publisher.
8. Brown, J. W, Heath, D., Morris, T. L, and Whitaker, W.: Tricuspid Atresia, Brit. Heart J. 18: 499, 1956.
9. Neill, C. A.: Quoted by Keith, Rowe, and Vlad.[6]

PRESSURE CONDITIONS IN THE PULMONARY CIRCULATION DURING CARDIAC BYPASS BY DOUBLE PUMPS

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In searching for reliable methods of cardiac bypass for open cardiac surgery, several techniques for the oxygenation of blood have been tried. Isolated homologous and heterologous lungs were used (Mustard[8, 9]) as well as autogenous lungs (Wesolowsky and Welch,[14] Read and co-workers,[12] Blanco, Schaefer, and Bailey,[1] Drew,[5, 6] Shields and Lewis,[13] Mustard, Sapirstein, and Pay,[10] Helmsworth and associates[7]). The use of the autogenous lungs for oxygenation has been technically rather complicated, especially in cardiac malformations such as septal defects. The interest for this method diminished when promising artificial oxygenators were developed. However, the artificial oxygenators have their limitations and, with long periods of extracorporeal circulation, the mortality is high. There seems experimentally to be a decrease in the diffusion capacity of the lungs (Pitzele and Senning[11]) which is a serious problem especially in patients with low pulmonary reserve, for example, with ventricular septal defect combined with pulmonary hypertension. The cause of this decrease in pulmonary diffusion capacity is not known but may be due to the fact that the lung is the only organ that is not perfused during the period of bypass. The trend has been therefore to find a suitable technique of using the autogenous lung in cardiac bypass.

A right-sided bypass can be suspected of having an unfavorable effect on the pulmonary vascular system as pulmonary edema often appears after bypass (Blanco and associates[2]). These experimental series have been made to study changes in pressures in the pulmonary circulation during cardiac bypass by an automatic double pump, using gravity drainage and the autogenous lung for blood oxygenation.

TECHNIQUE

Adult mongrel dogs, weighing 13 to 29 kilograms, were anesthetized with intravenous Pentothal intubated, and ventilated with an Engström respirator.

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The femoral arterial pressure was recorded. Thoracotomy was made through the fourth intercostal space.

Bypass was performed with a modification of the pump used in the Crafoord-Senning heart-lung machine* (Crafoord, Norberg, and Senning[3]) (Fig. 1). Eleven experiments were performed at normal body temperature. In nine experiments, the body temperature was lowered to about 20° C. with a disposable

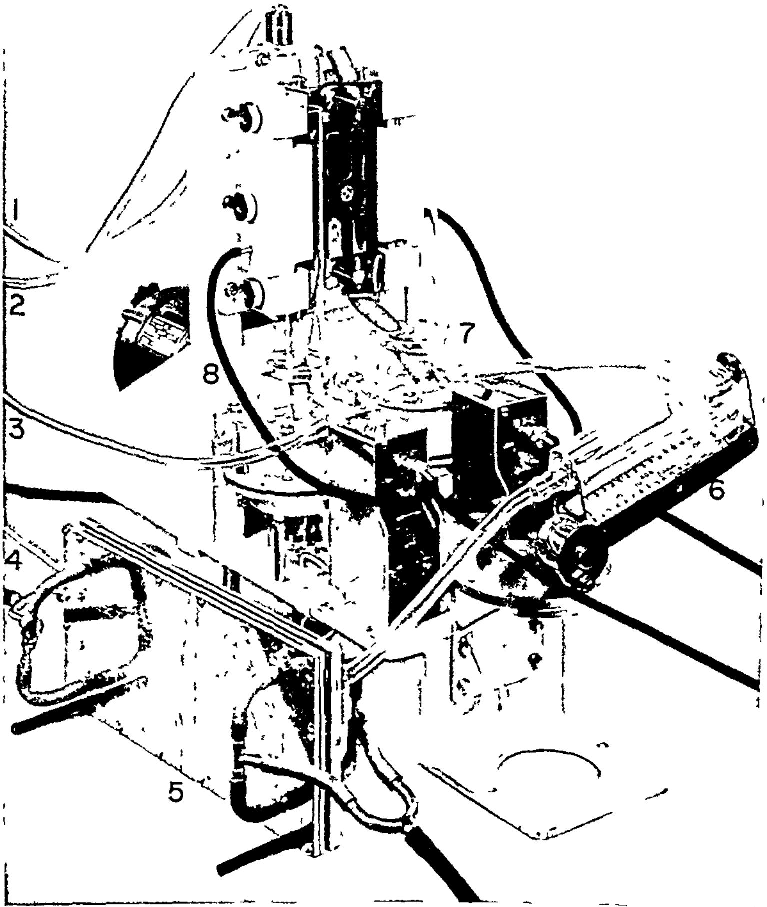

Fig. 1.—Double pump for cardiac bypass. *1*, Systemic arterial line. *2*, Pulmonary arterial line *3*, Systemic venous line. *4*, Pulmonary venous line. *5*, Heat exchanger *6*, Flow meter. *7*, "Left heart" regulation vessel *8*, "Right heart" regulation vessel.

heat exchanger in the "venous" side of the left heart pump. This heat exchanger consists of a thin-walled (15 by 30 cm.) plastic bag placed between two metal plates cooled by tap water. The distance between the metal plates can be adjusted from 1 to 4 mm. to regulate the resistance. Heparinized blood (25 mg. per 400 c.c. blood) was used to fill the system and the dog received

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*Manufactured by AGA, Lidingö, Sweden.

4 mg. per kilogram of body weight of heparin. Bypass was, in these experiments, started simultaneously in both circuits. Bypass of the right heart was made, draining the auricle by gravity to the reservoir of the pump through an intercalated flowmeter of rotameter type. The blood was pumped to the pulmonary artery by a cannula introduced through the outflow tract of the right ventricle. During bypass the pulmonary artery was strangulated round the inserted cannula. In four experiments, one pulmonary artery was occluded and perfusion done only to the other lung.

The left heart was bypassed in a similar way. Blood was drawn from the left atrium through a cannula via the heat exchanger into the reservoir of the arterial pump and pumped back to the systemic circulation through the subclavian artery. The pumps automatically pumped back all blood received from the atria. The flow was thus mainly dependent on the total circulating blood volume in the machine and the body. It was kept at a level where the blood pressure during bypass was about the same as before the perfusion, except in the nine experiments in which hypothermia was used. In six of these experiments, the flow was diminished during cooling from 50 to 30 ml. per kilogram of body weight per minute. Undesired variations in flow were corrected by adjustment of the blood volume.

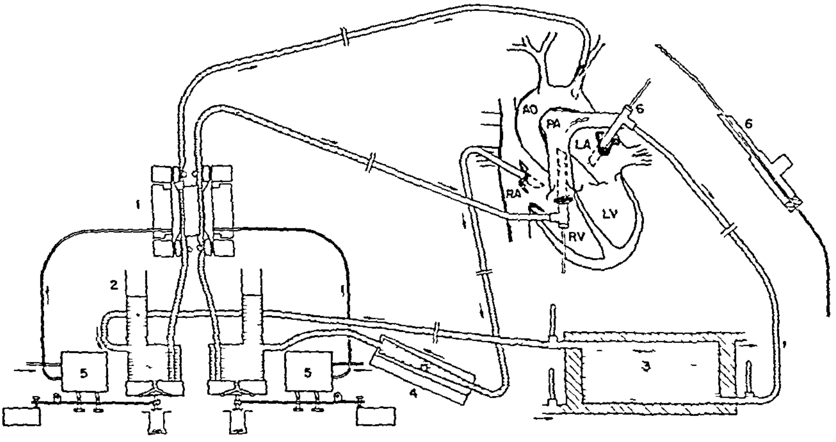

Fig. 2.—Schematic illustration of cardiac bypass by double pump. *1*, Double pump. *2*, "Left heart" regulation vessel. *3*, Heat exchanger. *4*, Flow meter. *5*, Pump cuff-pressure regulating valve. *6*, Left auricular cannula with inserted pressure-recording cannula.

Pressures in the pulmonary artery, left atrium and femoral artery were recorded with the reference point 8 cm. above the operating table by cannulae inserted in the pulmonary artery, the left atrium, and the femoral artery (Fig. 2).

The bypass lasted 60 minutes in eleven experiments at normothermia, and 80 minutes in eight hypothermia experiments, and 120 minutes in one. Cooling and rewarming periods were 20 to 35 minutes. After finishing bypass, protamine chloride was given until coagulation time was about 5 minutes; the blood volume was adjusted to the calculated pre-perfusion value.

RESULTS

Normothermia.—There were eleven bypass experiments under normothermia. In Fig. 3 the curves represent the average arterial, pulmonary artery, and left atrial pressures as well as the flow during bypass.

At an average flow rate of 50 ml. per kilogram of body weight per minute, the arterial pressure was maintained at the same level as before bypass. After perfusion was finished, a fall in arterial pressure was constant. It returned to normal when the blood volume was corrected; usually a blood transfusion of 100 to 200 ml. was given.

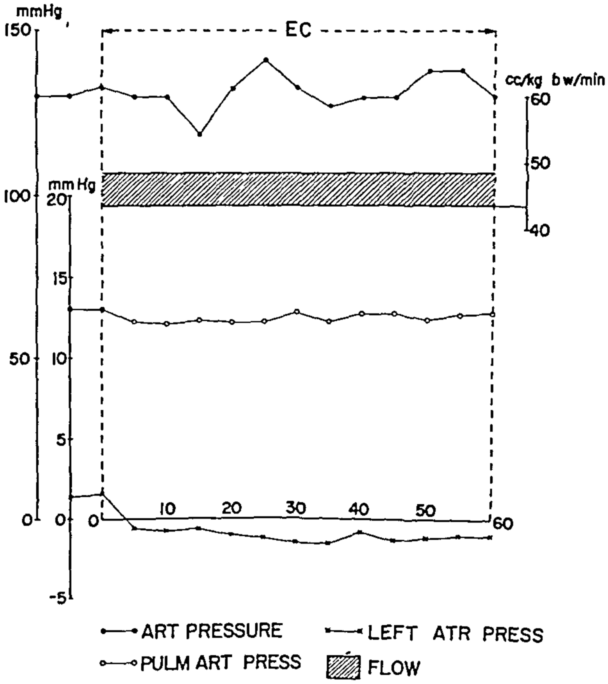

Fig. 3.—Average mean values of pressure in systemic artery, pulmonary artery, and left atrium during bypass with double pump in eleven experiments in which blood flow was kept constant and body temperature normal.

The pre-perfusion pressure in the pulmonary artery was about 13 mm. Hg. It remained stable with insignificant fluctuations throughout the experiments in all but 1 dog. This dog had a pulmonary artery pressure of 25 mm. Hg prior to the bypass, which rose to a maximum of 32 mm. Hg during bypass and fell to 27 mm. Hg at the end of it. In this dog, the flow was 80 ml per kilogram of body weight per minute. In the case in which one pulmonary artery was clamped, the pressure in the main pulmonary artery did not increase significantly.

The pressures found in the left atrium averaged 1.5 to 2 mm Hg before bypass and dropped to –0.5 mm. Hg when perfusion started and to –1 mm Hg at the end of it. After perfusion was finished it immediately became normal.

There were no signs of pulmonary edema in any of the perfused normothermic dogs.

Hypothermia.—In nine experiments, extracorporeal circulation was combined with cooling. Fig. 4 shows the recordings of one typical experiment in which the flow was allowed to fall. In the experiment shown in Fig. 5, the flow was kept constant. Cooling was performed during the first 20 to 25 minutes of perfusion and rewarming during the last 25 to 30 minutes. With falling temperature, the pressures fell in the systemic arteries, the pulmonary artery, and the left auricle. In three experiments, however, there was a short rise in arterial and pulmonary artery pressure during the first minutes after the start of perfusion with cold blood, as is shown in Fig. 5.

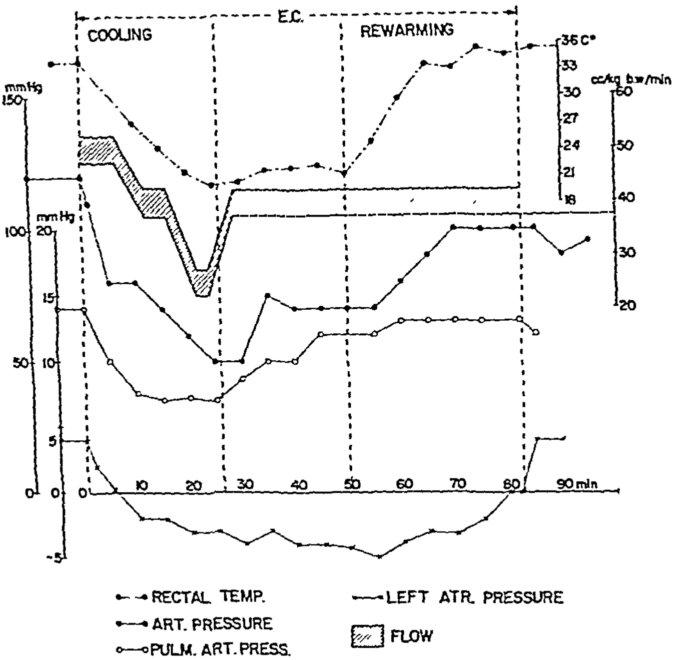

Fig. 4.—Mean values of pressure in systemic artery, pulmonary artery, and left atrium, blood flow and rectal temperature during bypass with double pump combined with internal cooling. A typical experiment in which the blood flow was allowed to fall.

During rewarming, the pressures rose and afterward showed the same pattern as in the experiments without hypothermia.

There were no signs of pulmonary edema in any of the perfused hypothermic dogs.

DISCUSSION

It seems possible that the high mortality after long periods of extracorporeal circulation is caused, in some cases, partly by a decreased pulmonary diffusion capacity due to the fact that the lung is not perfused during bypass, or partly because the capillaries are occluded by blood particles, or partly because of a general effect of blood trauma. These injurious factors can be avoided or diminished by excluding the artificial oxygenator through using the autogenous lung as an oxygenator. The lungs are then perfused and the blood trauma from artificial oxygenation is avoided. In combination with cooling, the perfusion volume can be decreased and, as the circulation is supported by pumps,

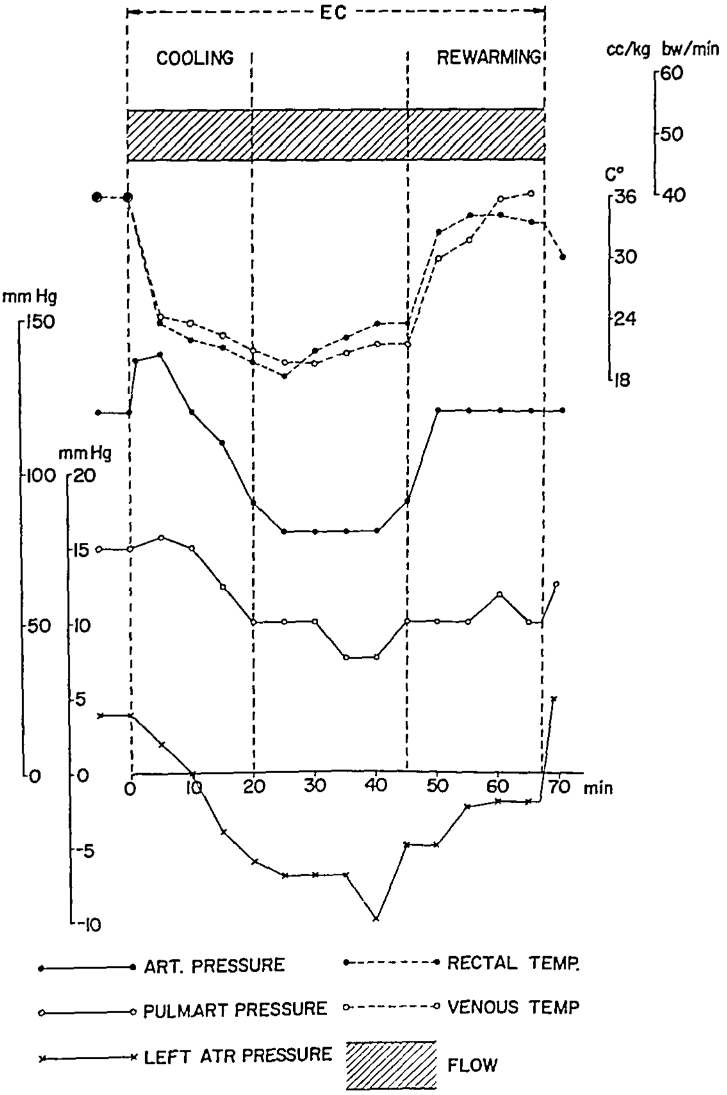

Fig. 5.—Mean values of pressure in systemic artery, pulmonary artery, and left atrium, as well as blood flow, rectal and venous temperatures during bypass with double pump combined with internal cooling. A typical experiment in which the blood flow was kept constant.

deep hypothermia can be applied. The flow can then be extremely small and periodically arrested, and thus the blood trauma also is diminished in the pumps. This technique seems to be of special importance in coronary surgery when long extracorporeal circulation periods are necessary.

This experimental series has been performed in order to see if pulmonary vascular changes occur during cardiac bypass performed by double pumps, with or without internal cooling.

In the series of eleven experiments at normothermia, there were no changes in the pulmonary artery pressure, if the starting pressure was normal and the flow was kept at a level where the blood pressure in the systemic arteries was the same as before bypass. As the collecting vessels of the pump were placed at a low level, the pressure in the left atrium fell below zero in the central part of the atrium. This minimized filling of the left ventricle from the atrium. After finished perfusion, the left atrial pressure immediately reverted to the pre-perfusion value. The pressure showed an insignificant rise during bypass at a flow of 80 ml. per kilogram of body weight in only 1 dog with slight pulmonary hypertension before bypass. This returned to normal, as in the other experiments, after perfusion was ended. No changes in the pulmonary vascular resistance during bypass were found in this series of eleven experiments.

In the other series of nine experiments, in which bypass with double pumps was combined with internal cooling to a body temperature of 20° C., the flow was kept constant in three experiments, and diminished during the period of cooling in six experiments. In all experiments, there was a decrease in the pulmonary artery pressure.

The pressure in the left atrium was recorded in the region of the mitral valves where the cannulae hinder the atrium from collapsing, thus making a negative pressure possible. This pressure is not, on the other hand, representative for the pulmonary veins. They collapse when the pressure is zero and the thorax is open. The increased pressure gradient between the pulmonary artery and the left atrium thus is an artefact only; there is no real increase in pulmonary vascular resistance. When the temperature of the experimental animal is normalized and the perfusion is ended, the pulmonary artery and left atrial pressures have reached their original pre-perfusion levels.

This experimental series has been part of our training program. Therefore the mortality has been high because of technical errors. When the most experienced among us performed the perfusion, 6 animals out of 8 survived after 1 hour of perfusion; and two out of three survived in experiments when there was 80 minutes of perfusion with the animals under hypothermia. The cause of death was postoperative bleeding and infection.

Experimentally there were no signs of pulmonary circulatory damage when this technique of cardiac bypass was applied. The method seems to have its application in clinical cardiac surgery.

REFERENCES

1. Blanco, G., Schaefer, J., and Bailey, C. P.: Clinical Use of the Autogenous Lung in Cardiac Bypass, III World Congress of Cardiology, Brussels, 1958, Abstracts of Communications 509.
2. Blanco, G., Oca, C., Laguna, S., Nuñez, L., Schaefer, J. and Bailey, C.: Autogenous Lung Oxygenation During Cardiac Bypass. Experimental Studies and Clinical Application in Aortic Valve Surgery, Am. J. Cardiol. 2: 302, 1958.
3. Crafoord, C., Norberg, B., and Senning, Å.: Clinical Studies in Extracorporeal Circulation With a Heart-Lung Machine, Acta chir. scandinav. 112: 220, 1957.

4. Dodrill, F. D., Marshall, N., Nyboer, J., Hughes, C. H., Derbyshire, A. J., and Stearns, A. B.: The Use of the Heart-Lung Machine Apparatus in Human Cardiac Surgery, J. THORACIC SURG. 33: 60, 1957.
5. Drew, C. E., Keen, G., and Benazon, D. B.: Profound Hypothermia, Lancet 1: 745, 1959.
6. Drew, C. E., and Anderson, I. M.: Profound Hypothermia in Cardiac Surgery, Lancet 1: 748, 1959.
7. Helmsworth, J. A., Shabetai, R., Cole, W. R., Neely, J. C., Albers, J. E., and Gonzalès L. L.: A Method of Cardiac Bypass With Autogenous Oxygenation, Surgery 45: 129, 1959.
8. Mustard, W. T., and Chute, A. L.: Experimental Intracardiac Surgery With Extracorporeal Circulation, Surgery 30: 684, 1951.
9. Mustard, W. T., Chute, A. L., and Simmons, E. H.: Further Observations on Experimental Extracorporeal Circulation, Surgery 32: 803, 1952.
10. Mustard, W. T., Sapirstein, W., and Pav, D.: Cardiac Bypass Without Artificial Oxygenation, J. THORACIC SURG. 36: 479, 1958.
11. Pitzele, S., and Senning, Å.: Unpublished data.
12. Read, R. C., Vane, M. D., Georges, P., Cohen, M., and Lillehei, W. C.: Cardiac Bypass Using Autogenous Lung For Oxygenation, Surgery 40: 840, 1956.
13. Shields, T. W., and Lewis, F. J.: Rapid Cooling and Surgery at Temperatures Below 20° C., Surgery 46: 164, 1959.
14. Wesolowsky, A., and Welch, S.: Experimental Maintenance of the Circulation by Mechanical Pumps, Surgery 31: 769, 1952.

SYSTEMIC HYPERTENSION COMPLICATING THE LIGATION OF PATENT DUCTUS ARTERIOSUS

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THE development of sclerotic changes in the pulmonary vessels and consequent pulmonary hypertension are common complications of patent ductus arteriosus. If these sclerotic changes are far advanced, the blood pressure in the pulmonary artery may approximate the pressure of the aorta and the original left-to-right shunt becomes "bi-directional" or even reversed. In cases of severe pulmonary hypertension, the ductus serves as a vent which decompresses the overloaded lesser circulation.[1, 2, 4, 5, 8, 9, 16, 17] The dangers of ligation of the ductus in such conditions were recognized early.[8-11, 18] The closure of this "emergency outlet" may lead to an immediate increase of the blood pressure in the pulmonary artery and cause an acute insufficiency of the right ventricle, which is usually fatal.

The pressure relations in the systemic circulation are less affected by the pressure of the ductus.[18] Because of the decrease of the total systemic circulatory resistance, the diastolic pressure is usually low; the systolic pressure remains normal.[14, 15] Following ligation of the ductus, the diastolic pressure returns to normal. Holman has described an increase also in the systemic systolic arterial pressure following operative closure of patent ductus arteriosus. He attributed this temporary rise in pressure to increased blood volume. The pressures in these cases returned to normal when the blood volume became normal.[7-9]

One of our patients, on whom a surgical closure of a patent ductus arteriosus was performed, experienced a very unusual complication, i.e., the development of an acute, severe, permanent systemic hypertension.

CASE REPORT

A 38-year-old white woman was admitted on May 18, 1957, to the Department of Thoracic Surgery, Mercy Hospital. She was known to have had heart disease since infancy. Her symptoms were those of exertional dyspnea, some pain in the mid-sternal area, palpitation, and nonproductive cough. These symptoms became more pronounced during the 4 months previous to admission.

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Physical examination of the cardiovascular system showed moderate enlargement of the heart. The pulmonary second sound was somewhat accentuated and split. There was a systolic-diastolic thrill and a continuous systolic-diastolic machinery murmur in the left second and third interspaces parasternally. The pulse rate was 86 per minute; blood pressure in the left arm 158/65 mm. Hg. Peripheral pulses were easily palpable and there were no symptoms of congestive heart failure.

Routine laboratory findings were essentially negative. Chest x-ray examination showed increased pulmonary vascular markings. The heart was moderately enlarged, due primarily to left ventricular enlargement. There was also a dilatation of the ascending aorta and aortic arch. The pulmonary conus was prominent and pulsated expansively. Electrocardiogram showed depressed S-T segments in Leads I-III, negative T waves in Leads II-III, diphasic T waves in V_5-V_6. There were frequent ventricular extrasystoles.

Cardiac catheterization revealed evidence of a patent ductus arteriosus with significant left-to-right shunt (Fig. 1). The results were also suggestive of a moderate incompetence of the pulmonary valve.

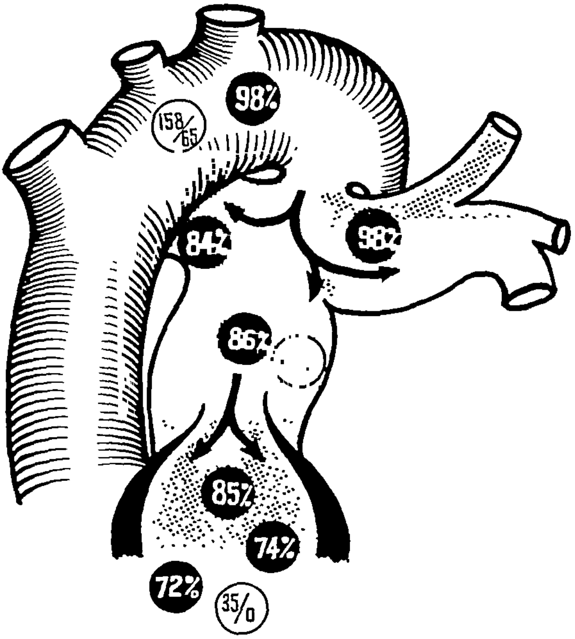

Fig. 1.—Schematic presentation of the preoperative hemodynamic conditions. The white circles show the blood pressure in mm. of mercury, the black circles the oxygen saturation of the blood.

At operation, a large patent ductus arteriosus (approximately 1 cm. in diameter) was found. This was occluded by two simple ligatures and multiple transfixion sutures. Immediately following the closure of the ductus, the anesthetist reported a 35 mm. Hg increase in the systolic and 40 mm. Hg increase in the diastolic blood pressure; otherwise the patient tolerated the procedure well. There were no changes in the force or rhythm of the heart action.

Two hours after operation the patient's blood pressure rose to 190/110 mm. Hg. The pulse rate increased to 140 per minute. Apresoline (25 mg.) and Thorazine (50 mg.) were administered, after which the blood pressure decreased to 160/90 mm. Hg, but within 4 hours it was elevated again to 210/120. The patient also had a protodiastolic gallop rhythm and complained of general discomfort. She had several attacks of paroxysmal dyspnea. After 24 hours of continuous Apresoline and Thorazine therapy, she showed some improvement. The blood pressure remained relatively stabile between 170 to 160 systolic values, and dyspnea and orthopnea became less pronounced. The Apresoline and Thorazine were discontinued, but restarted after the blood pressure rose to 220/135 mm. Hg, and the patient developed a moderate attack of pulmonary edema. She remained on Apresoline, Thorazine, Hydryllin tablets, low sodium diet, and digitalis for 2 weeks. She was then discharged with a blood pressure of 175/100 mm. Hg and in relatively good condition.

Afterward the patient was closely followed. She reported several attacks of tachycardia, precordial pain, and paroxysmal dyspnea. The blood pressure varied between 145/90 and 190/110 mm. Hg. Peroral digitoxin annd Apresoline were continued. She is now able to perform limited physical activity.

CONCLUSIONS

The appearance of a severe systemic hypertension in the immediate postoperative period is an unusual complication following ligation of a patent ductus arteriosus. A reasonable explanation of this phenomenon is that outside of the possible increase in the blood volume[7-9] the patient had a narrowing of the systemic arterioles *before* surgery. However, the increase in the circulatory resistance did not manifest itself in hypertension because the systemic circulation was connected through the patent ductus with a low-pressure, large capacity vascular pool, i.e., the pulmonary circulatory system. Similar conditions have been created by the production of peripheral arteriovenous fistulae in clinical and experimental hypertension.[3, 6, 12, 13] When this patient's ductus arteriosus was occluded, the "latent" hypertension became manifest. This hypothesis is supported by the fact that the patient had a moderate elevation of the systemic blood pressure even in the presence of the patent ductus arteriosus. The preoperatively determined "corrected" systemic circulatory resistance was found to be elevated and gives additional support to the hypothesis.

The situation is very similar to that which exists in the presence of a patent duct with right-to-left shunt, the difference being that it is not the overloading of the pulmonary system but the systemic circulation which, in this instance, threatens the patient's life. From this case the conclusion may be drawn that in the presence of an elevation of the systemic arterial blood pressure, the ligation of a patent ductus should be performed with caution, as the occlusion of the "emergency vent" may lead to an increase of the blood pressure and a sudden overloading of the systemic circulation.

SUMMARY

The authors present a case of a 38-year-old woman with a patent ductus arteriosus accompanied by elevation of the systemic circulatory resistance and moderate increase in the systemic arterial blood pressure. The ligation of the ductus was complicated by an acute, severe systemic arterial hypertension.

An analogy is made between this condition and the situation that exists when a patent ductus arteriosus is occluded in the presence of pulmonary hypertension. The patent ductus arteriosus may serve in both instances as an emergency vent, and its occlusion may lead to serious consequences in either case.

REFERENCES

1. Campbell, M. J., and Hudson, R. D.: Patent Ductus Arteriosus With Reversed Shunt Due to Pulmonary Hypertension, Guy's Hosp. Rep. London 100: 26, 1951.
2. Campbell, M. J. and Hudson, R. D.: Disappearance of Continuous Murmur in Patent Ductus Arteriosus, Guy's Hosp Rep. London 101: 32, 1952.
3. Deterling, R. A., and Essex, H. E.: Experimental Renal Hypertension and Its Course Following Production of a Peripheral Arteriovenous Fistula, Ann. Surg. 132: 129, 1950.
4. DuShane, J. W., and Montgomery, G. E., Jr.: Patent Arteriosus With Pulmonary Hypertension and Atypical Clinical Findings, Proc. Staff Meet. Mayo Clin. 23: 505, 1948.
5. Fishman, L., and Silverthorne, M. C.: Persistent Patent Ductus Arteriosus in Aged Including Report of Oldest Case on Record With Diagnosis Confirmed Post Mortem, Am. Heart J. 41: 762, 1951.
6. Hawthorne, E. W., Brownlee, G. V., and Pogue, W. G.: Arterial Pressure Changes in Experimental Renal Hypertensive Dogs Following Production of Femoral Arteriovenous Fistula, Am. J. Physiol. 180: 65, 1955.
7. Holman, E.: The Anatomic and Physiologic Effects of an Arteriovenous Fistula, Surgery 8: 362, 1940.
8. Holman, E.: The Surgery of Congenital Malformations of the Heart and Great Vessels, Standford M. Bull. 6: 227, 1948.
9. Holman, E., Gerbode, F., and Purdy, A.: The Patent Ductus. A Review of Seventy Five Cases With Surgical Treatment, Including an Aneurysm of the Ductus and One of the Pulmonary Artery, J. THORACIC SURG. 25: 111, 1953.
10. Hultgren, H., Lebrer, A., Purdy, A., Holman, E., and Gerbode, F.: Syndrome of Patent Ductus Arteriosus With Pulmonary Hypertension, Circulation 8: 15, 1953.
11. Johnson, R. E., Wermer, P., Kuschner, M., and Cournand, A.: Intermittent Reversal of Flow of Patent Ductus Arteriosus. Physiologic Study With Autopsy Findings, Circulation 1: 1293, 1950.
12. Lian, C., and Welti, H.: Cited by Hawthorne, Brownlee and Pogue.[6]
13. Petri, G.: Personal communication.
14. Sanger, P. W., Taylor, F. H., and Robicsek, F.: The Diagnosis and Treatment of Coronary Arteriovenous Fistula, Surgery 48: 344, 1959.
15. Sanger, P. W., Robicsek, F., Taylor, F. H., Magistro, R., and Foti, E.: Observations on Pulmonary Vasomotor Reflexes, J. THORACIC SURG. 37: 773, 1959.
16. Shapiro, M. J.: Preoperative Diagnosis of Patent Ductus Arteriosus, J. A. M. A. 126: 934, 1944.
17. Smith, G.: Patent Ductus Arteriosus With Pulmonary Hypertension and Reversed Shunt, Brit. Heart J. 16: 233, 1954.
18. Taylor, B. E., Pollack, A., Burchell, H., Clagett, T., and Wood, W.: Studies of Pulmonary and Systemic Arterial Pressure in Cases of Patent Ductus Arteriosus With Special Reference to Effects of Surgical Closure, J. Clin. Invest. 29: 745, 1950.
19. Temesvari, A., and Robicsek, F.: Beitrage zur Nevosen Regulation der Kleinen Kreislaus Wirkung des Pendiomids beim Experimentellen aorto pulmonalen Shunt. Thoraxchirurgie 4: 489, 1957.

A METHOD FOR CONTROLLING A PATENT DUCTUS ARTERIOSUS DURING OPEN-HEART SURGERY

Philip Glotzer, M.D., and Allan E. Bloomberg, M.D.,
New York City, N. Y.

THE RECOGNITION and control of a patent ductus arteriosus during cardiac bypass with cardioplegia is essential for a successful run on the pump-oxygenator.[1] Failure to obtain control of the ductus results in massive and rapid distention of the right heart, severe pulmonary congestion, and death.

On occasion a patent ductus may be unrecognized because of misinterpretation of operative physical findings or be virtually impossible to control safely because of dense pericardial and pleural adhesions. We recently faced this situation, and herein is presented a method which allowed successful control of the ductus.

The patient was an 11½-year-old girl who was admitted to the hospital for the open-heart repair of a tetralogy of Fallot lesion. Seven years previously, this child had undergone a transventricular pulmonary valvulotomy at this hospital. At that time, a ductus had been looked for and not found. At this operation very dense pleural and pericardial adhesions were present. A thrill over the pulmonary artery was thought to be due to persistent pulmonic stenosis and pulmonic insufficiency.

The moment cardiac arrest was produced, a rapid dilatation of the right ventricle occurred. This was relieved by immediate right ventriculotomy. The resulting continuing blood loss was alarming because of the rapid fall in the reservoir level of the oxygenator. Control of the blood loss was then immediately obtained by occluding the pulmonic opening of the ductus with a finger passed into the pulmonary artery (Fig. 1). The blood level in the reservoir instantly stabilized. With the finger in place, the ventriculotomy was continued out into the pulmonary artery to the level of the ductus. A purse-string suture was placed around the ductus orifice, which resulted in complete control of the bleeding (Fig. 2). The operation then proceeded with a direct approach to the congenital intracardiac defects.

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REFERENCES

1. Campbell, M. J., and Hudson, R. D.: Patent Ductus Arteriosus With Reversed Shunt Due to Pulmonary Hypertension, Guy's Hosp. Rep. London **100**: 26, 1951.
2. Campbell, M. J. and Hudson, R. D.: Disappearance of Continuous Murmur in Patent Ductus Arteriosus, Guy's Hosp. Rep. London **101**: 32, 1952.
3. Deterling, R. A., and Essex, H. E.: Experimental Renal Hypertension and Its Course Following Production of a Peripheral Arteriovenous Fistula, Ann. Surg. **132**: 129, 1950.
4. DuShane, J. W., and Montgomery, G. E., Jr.: Patent Arteriosus With Pulmonary Hypertension and Atypical Clinical Findings, Proc. Staff Meet. Mayo Clin. **23**: 505, 1948.
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6. Hawthorne, E. W., Brownlee, G. V., and Pogue, W. G.: Arterial Pressure Changes in Experimental Renal Hypertensive Dogs Following Production of Femoral Arteriovenous Fistula, Am. J. Physiol. **180**: 65, 1955.
7. Holman, E.: The Anatomic and Physiologic Effects of an Arteriovenous Fistula, Surgery **8**: 362, 1940.
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9. *Holman, E., Gerbode, F., and Purdy, A.: The Patent Ductus.* A Review of Seventy-Five Cases With Surgical Treatment, Including an Aneurysm of the Ductus and One of the Pulmonary Artery, J. Thoracic Surg. **25**: 111, 1953.
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14. Sanger, P. W., Taylor, F. H., and Robicsek, F.: The Diagnosis and Treatment of Coronary Arteriovenous Fistula, Surgery **48**: 344, 1959.
15. Sanger, P. W., Robicsek, F., Taylor, F. H., Magistro, R., and Foti, E.: Observations on Pulmonary Vasomotor Reflexes, J. Thoracic Surg. **37**: 773, 1959.
16. Shapiro, M. J.: Preoperative Diagnosis of Patent Ductus Arteriosus, J. A. M. A. **126**: 934, 1944.
17. Smith, G.: Patent Ductus Arteriosus With Pulmonary Hypertension and Reversed Shunt, Brit. Heart J. **16**: 233, 1954.
18. Taylor, B. E., Pollack, A., Burchell, H., Clagett, T., and Wood, W.: Studies of Pulmonary and Systemic Arterial Pressure in Cases of Patent Ductus Arteriosus With Special Reference to Effects of Surgical Closure, J. Clin. Invest. **29**: 745, 1950.
19. Temesvari, A., and Robicsek, F.: Beitrage zur Nevosen Regulation der Kleinen Kreislaus. Wirkung des Pendiomids beim Experimentellen aorto-pulmonalen Shunt. Thoraxchirurgie **4**: 489, 1957.

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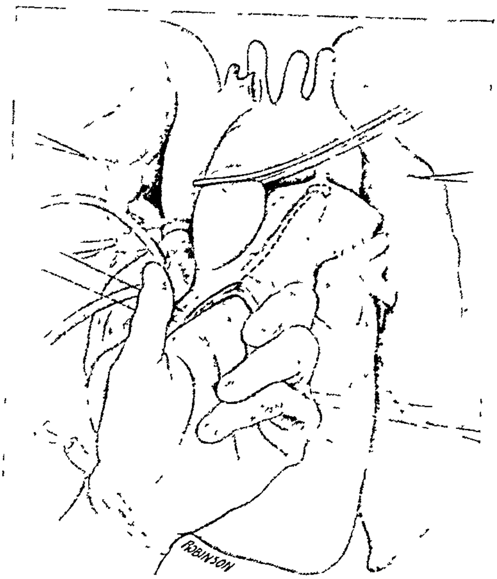

Fig. 1.—Control of the ductus is obtained by occluding the pulmonic orifice with the finger. The dotted line shows the proposed line of incision.

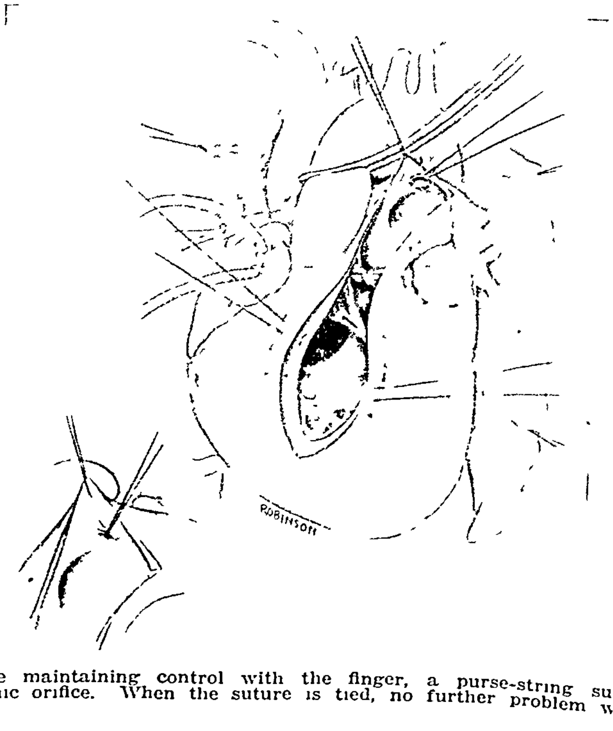

Fig. 2.—While maintaining control with the finger, a purse-string suture is placed around the pulmonic orifice. When the suture is tied, no further problem with the ductus exists.

REFERENCE

1. Kirkland, J. W., and Silver, A. W.: Technique of Exposing the Ductus Arteriosus Prior to Establishing Extracorporeal Circulation, Proc. Staff Meet. Mayo Clin. 33: 423-425, 1958.

CONGENITAL DEFICIENCY OF THE PERICARDIUM

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ALTHOUGH the 2 cases to be reported here apparently represent the one hundredth and one hundred first of a colorful series that began in 1559,[1] it is anticipated that with an increasing number of thoracotomies and constant improvement in radiologic techniques, the condition may soon forfeit its appellation of "a rarity."

Ellis, Leeds, and Himmelstein[1] have recently described 2 patients who had complete absence of the left parietal pericardium. The reader is referred with enthusiasm to their excellent article which includes interesting diagnostic techniques and a classification of pericardial defects.

As has been noted many times in the literature, pericardial defects are seldom diagnosed or encountered prior to autopsy. We would like to report 2 cases of partial absence of the left parietal pericardium in which the diagnosis was suggested before operation and confirmed by thoracotomy. It is our feeling that these cases demonstrate certain characteristic features which may be of value in the diagnosis and treatment of patients with pericardial defects.

CASE REPORTS

CASE 1.—A. H. W., 244120, a 22-year-old Negro man, was admitted to the U. S. Naval Hospital, Chelsea, Mass., on Feb. 14, 1958, for evaluation of a pulsatile mass along the upper third of the left cardiac border. Three years prior to admission a routine 70 mm. photofluorogram revealed an abnormal cardiac configuration in the then asymptomatic patient. Cardiac fluorography and radiography on June 27, 1955, revealed the heart to be globular in appearance with a definite increase in the size of the upper third of the left cardiac border which appeared to be pulsatile and was assumed to represent the pulmonary artery. No ventricular enlargement was noted, nor did the left atrium appear selectively enlarged. The aorta was reported as small and the pulmonary vasculature normal. No abnormal physical findings were recorded and the electrocardiogram was interpreted as being within normal limits. Following this examination the patient was returned to full duty aboard ship.

The occasion of his admission to this hospital was recurrent left anterior chest pain which was described as sharp and pressure-like, occurring both at rest and with exercise,

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The opinions herein expressed are those of the authors, and do not necessarily reflect the views of the Medical Department of the Navy or of the Naval Service at large.

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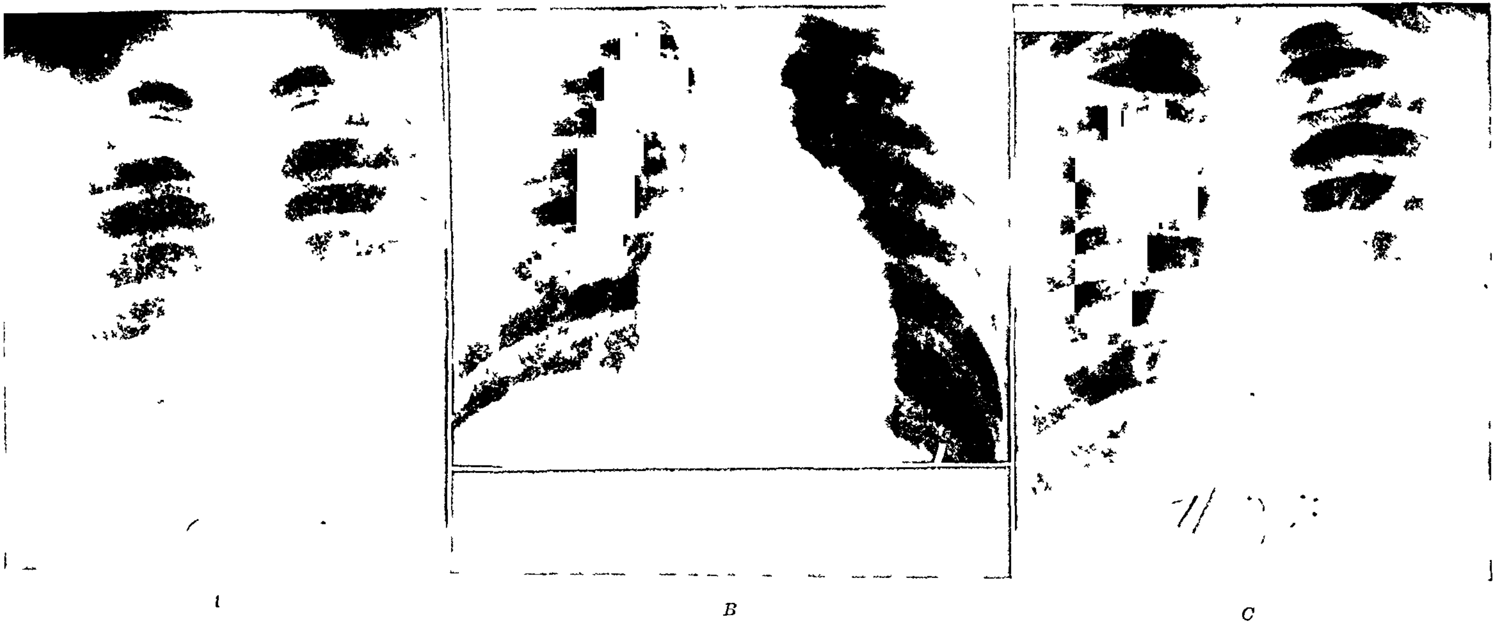

Fig 1 —Case 1 *A*, Preoperative posteroanterior roentgenogram of the chest showing characteristic left atrial appendage shadow *B* Angiocardiographic exposure demonstrating the relationship of the pulmonary artery to the left atrial appendage *C*, Postoperative posteroanterior roentgenogram of chest showing the persistence of the left atrial bulge minus the appendage

nonradiating, and of about 2 minutes' duration. This complex occurred several times a month and had been noted for approximately 2 years. The pain was unrelated to food intake, activity, or position. Other and possibly related symptoms included mild dyspnea on climbing two flights of stairs and mild syncope during extreme heat, both symptoms relieved by rest. The balance of the history was noncontributory.

Physical examination revealed a well-developed, well-nourished Negro man in no distress. Blood pressure was 126/72 mm. Hg, pulse 84, respirations 14, and temperature 98.6° F. Peripheral pulses were readily palpable and equal bilaterally, and there was no cyanosis, clubbing, or edema. A mild, left sternal border heave was palpable along with a tapping apical impulse, the point of maximum intensity being indistinct. Cardiomegaly was not present. The rate was 84 with a variable sinus arrhythmia and occasional premature contractions. A Grade 2 (of 6) blowing systolic murmur was audible along the left sternal border, maximal at the third intercostal space. A precordial friction-type sound could be heard on occasion with the patient standing and flexed 45 degrees at the waist. The remainder of the physical examination was entirely normal.

Laboratory studies, including blood chemistry, hemogram, urinalysis, serologic test for syphilis, C-reactive protein, anti-streptolysin-O titer, skin tests for tuberculosis and mycotic disease, and sickle cell preparations, were within normal limits. Electrocardiograms revealed frequent ventricular ectopic beats, some of which were not premature and suggestive of a sinus pause and ventricular escape beat, but were regarded as within normal limits.

Cardiac fluoroscopy again revealed a prominent bulge along the left upper heart shadow which had not apparently changed since the initial examination recorded in 1955. Expansile pulsation of the abnormal bulge was noted, but no cardiac chamber enlargement could be demonstrated in the examination made after a barium swallow.

On March 3, 1958, right heart catheterization was performed, and this revealed normal right cardiac hemodynamics without evidence of shunt. All accompanying determinations done during this study were within normal limits. On March 26, 1958, angiocardiograms were made in the posteroanterior and oblique projections with the use of 70 per cent Diodrast injected in the basilic vein through a Robb-Steinberg needle. The pulmonary artery and aorta could be definitely excluded as contributing to the abnormal shadow, but suspicion was cast upon the left pulmonary veins or an abnormally placed left atrial appendage.

The patient was then observed in several of his "attacks" during which he became faint, perspiring, and complained bitterly of pain in the left anterior chest. At the Cardiovascular-thoracic Conference, thoracotomy was advised.

On June 13, 1958, a left thoracotomy was performed through the left fifth interspace. The left upper lobe was found to be adherent to the left atrial appendage by firm adhesions, apparently of long standing, with some recent inflammation. The left atrium and its appendage lay well outside the normal confines of the cardiac mass. The appendage was elongated and sigmoid in shape. The pericardium was absent from the atrioventricular groove cephalad, and the cephalic margin was rolled and thickened. With each cardiac contraction the rolled margin massaged the left coronary and circumflex vessels. The pericardium, which was present, resembled an egg-cup, and the heart, the egg (see Fig. 3). There was no free left pericardial cavity, the remaining pericardium being adherent by fine but firm adhesions to the epicardium. Adhesions were divided and ligated where necessary. The left heart was explored digitally through an incision in the left atrial appendage. No abnormalities were detected by this maneuver. The appendage was amputated and the margins closed with interrupted and continuous silk sutures. Because of the anatomic position of the rolled pericardial edge and the adherent pericardium, a generous V-shaped excision of the pericardium over the right and left ventricles was performed. The patient recovered from the operative procedure without complication or difficulty. He stated during his postoperative course that the chest pains were no longer present. One year following operation he is well and working.

Case 2.—S. A. C., 253921, a 21-year-old sergeant in the USMC was admitted to the U. S. Naval Hospital, Chelsea, Mass., on June 1, 1959, with an undetermined diagnosis of

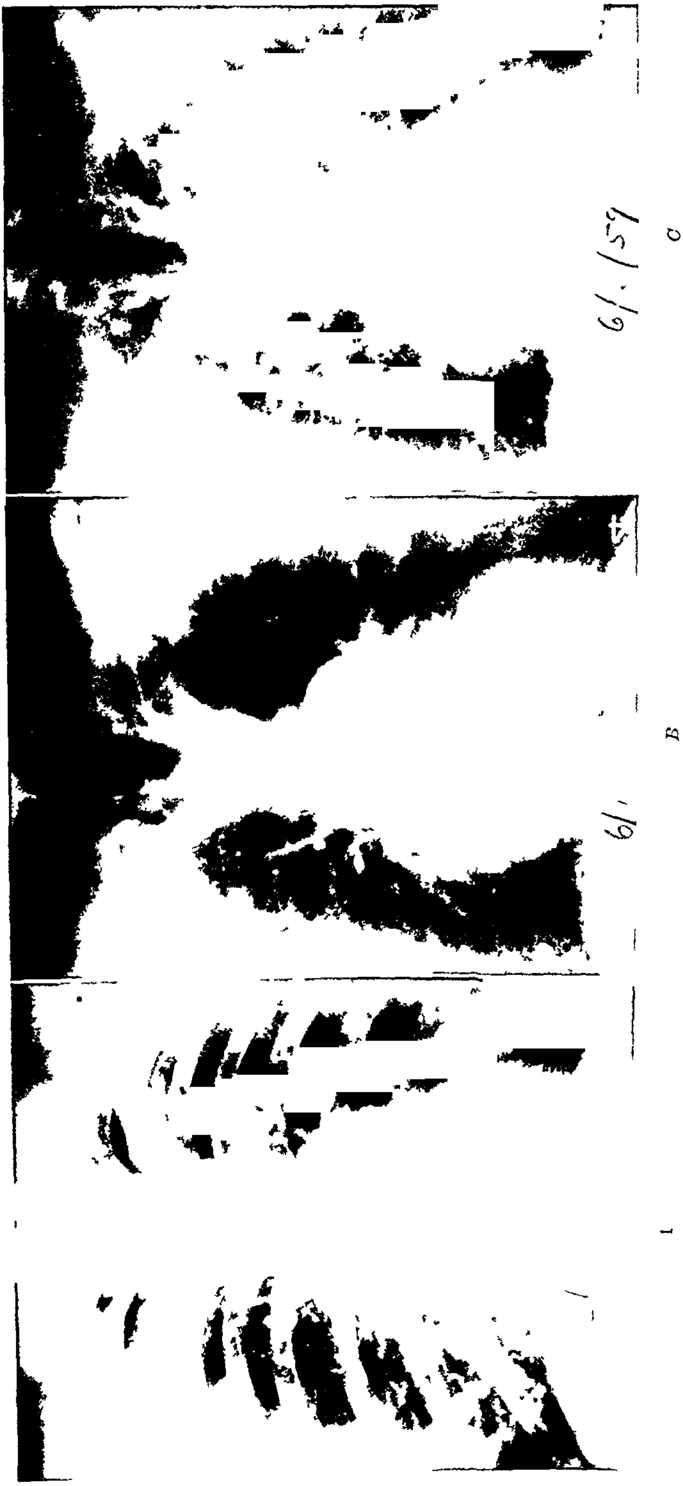

Fig 2 —Case 2 A, Preoperative posteroanterior roentgenogram of the chest showing characteristic left atrial appendage shadow B Angiocardiographic exposure showing the relationship of the pulmonary artery to the left atrial appendage C, Angiocardiographic exposure made during the left heart filling phase showing outlining of the left atrial appendage

dilatation of the pulmonary artery. This diagnosis was entertained following a routine chest x-ray examination which was reported as showing an abnormal pulmonary conus. He was entirely without symptoms, and physical examination was within normal limits. He was referred to the hospital for further studies referable to the abnormal shadow. This shadow consisted of a rather angular projection just lateral and inferior to the pulmonary artery, in the position of the left atrial appendage. In view of the previous case, a tentative diagnosis was made of herniated left atrial appendage due to partial absence of the pericardium.

Routine laboratory studies and further films of the chest exposed during barium swallow were not unusual. Angiocardiography with 70 per cent Sodium Urokon demonstrated that the pulmonary artery was innocent, but that the left atrial appendage became opacified at the proper interval and occupied the same position as the abnormal shadow noted on the plain films. At the Cardiovascular-thoracic Conference it was the consensus that although deficient pericardium was the most likely possibility, thoracotomy should be resorted to in order to rule out other lesions in this area.

On June 25, 1959, an exploratory thoracotomy was performed through the left fifth interspace, sparing the trapezius and rhomboid muscles. The ribs were spread just sufficiently to permit adequate visualization and palpation of the hilum and adjacent cardiac structures. As anticipated (see Fig. 4), the left atrial appendage resided partly outside the main cardiac mass, herniating through an upper pericardial window, and performing a considerable excursion with each cardiac systole. The left phrenic nerve comprised the medial margin of the pericardial defect. There were no adhesions, and the finger passed readily into the free pericardial cavity. Since the aperture seemed large enough to permit free action of the left atrial appendage and atrium, and too small to permit herniation or strangulation of the atrium or ventricle, no attempts were made to correct the condition, and the chest was closed. Postoperatively there were no complications, and the patient was discharged to duty July 28, 1959. Four months postoperatively he was having no difficulty.

EMBRYOLOGY

Studies by previous authors of the embryological antecedents of pericardial malformations have for the most part tended to incriminate the formation of the pleuropericardial and pleuroperitoneal folds. We agree with this concept and cite the case of Ladd[2] in its support. Ladd found a hernia of the Bochdalek type occurring in a patient who had deficiency of the pericardium. These lesions certainly involve the pleuroperitoneal and pleuropericardial folds. The theory has been entertained in addition that the growing lung pushes its way into the area deficient of pericardium, and so prevents the complete development of the pericardium. Our first case with lung firmly adherent to the heart may or may not bear out this latter concept.

CLINICAL AND DIAGNOSTIC FEATURES

It will be noted that Case 1 (Fig. 3), who had the larger defect and extensive inflammatory adhesions, had recurrent chest pain, and, at times, a pleuropericardial sound could be heard. The second patient, who had a smaller defect and no adhesions, was asymptomatic (Fig. 4). Right heart catheterization, having been normal in the first case, was not thought to be necessary in the second. Although we did not make use of diagnostic pneumothorax in either patient, we believe that it may be a valuable aid. In one postoperative film of the chest in the second patient, a small amount of right pericardial air may be seen, suggesting that use of preoperative pneumothorax would have been helpful in diagnosis.[1]

In Case 2 (Fig. 2, *B* and *C*), angiocardiography was diagnostic Those in Case 1 were less clear, but on careful inspection we felt that they were quite suggestive of the diagnosis in spite of technical factors producing a poor left side filling phase.

Fig 3

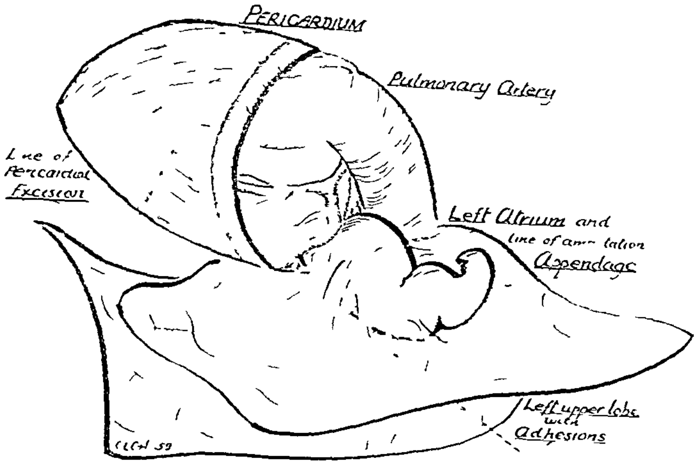
Pericardium
Pulmonary Artery
Line of Pericardial Excision
Left Atrium and line of amputation Appendage
Left upper lobe with Adhesions
LCH 59

Fig 4

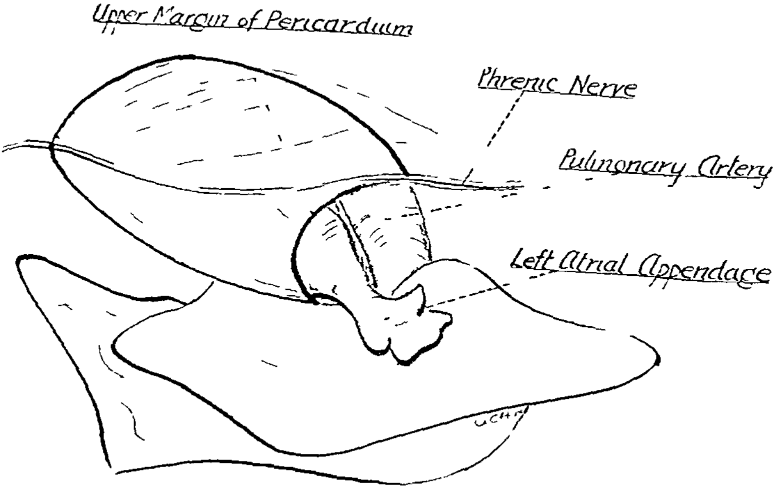

Fig 3—Sketch of operative findings (Case 1)
Fig 4—Sketch of operative findings (Case 2)

SURGICAL ASPECTS

In Figs 3 and 4 may be found the operative findings as drawn by the operator. Some consideration was given to the question of amputating the herniating left atrial appendage in the second case. Marked cardiac irregularity occurred when a clamp was applied to the base of the appendage, and the idea was forthwith abandoned.

CONCLUSIONS

1. It is our opinion, after a survey of the literature and the study of 2 patients who had similar diagnostic and surgical features, that congenital deficiency of the pericardium may be diagnosed with the aid of angiocardiography and pneumothorax.

2. Characteristic features in partial absence of the left pericardium are primarily radiologic, namely, an abnormal bulge in the region of the left atrial appendage in the standard posteroanterior roentgenogram, and the outlining of the appendage with contrast medium during the left heart filling phase of an angiocardiogram.

3. If the diagnosis seems clear, and the patient is, and has been, asymptomatic, surgical intervention may not be necessary. If symptoms are present, relief may follow thoracotomy, where atrial appendectomy, division of adhesions, and pericardioplasty may be performed.

REFERENCES

1. Ellis, K., Leeds, N. E., and Himmelstein, A.: Congenital Deficiencies of the Parietal Pericardium, Am. J. Roentgenol. 82: 125-137, 1959.
2. Ladd, W. E.: Congenital Absence of the Pericardium, New England J. Med. 214: 183, 1936.

Additional References

1. McGarry, R. A.: Patency of the Pericardium and Its Embryological Significance, Anat. Rec. 8: 43, 1914.
2. Beck, C. S.: Congenital Deficiency of the Pericardium, Arch. Surg. 22: 282-288, 1931.
3. Moore, R. L.: Congenital Deficiency of the Pericardium, Arch. Surg. 11: 765, 1925.
4. Watt, J. C.: Rare Congenital Deficiency of the Pericardium, Arch. Surg. 23: 995-1006, 1931.
5. Barsoum, H.: Absence of the Pericardium, Brit. M. J. 2: 666, 1935.
6. Ronka, E., and Tessmer, C.: Congenital Absence of the Pericardium, Am. J. Path. 20: 137, 1944.
7. Shafiroff, B.: Congenital Absence of the Pericardium, J. THORACIC SURG. 21: 30, 1951.
8. Venturini, A., and Pesci, A.: The Agenesis of the Pericardium, Arch. di Chirurg. del Torace 11: 189, 1957.

REPLACEMENT OF THE MAIN PULMONARY ARTERY BIFURCATION BY AUTOGENOUS PERICARDIUM

Lester R. Sauvage, M.D., Abraham M. Rudolph, M.D.,** and*
Robert E. Gross, M.D., Boston, Mass.

A TECHNIQUE has been developed for the successful one-stage experimental replacement of the distal main pulmonary artery, its bifurcation, and the major portions of both right and left pulmonary arteries that does not require the use of pumps, extracorporeal circulation, hypothermia, or circulatory interruption. This method was developed to allow for the study of pericardial autografts in the pulmonary arterial system. In this paper we shall outline the details of graft placement and shall describe the status of two such grafts over observation periods of 16 and 17 months, respectively.

METHOD

The method for extensive pulmonary artery resection and pericardial autograft replacement is shown in Fig. 1. The key step in this experimental technique is the transplantation of the left pulmonary artery to a position adjacent to the valve without producing stenosis of its orifice. We attempted this procedure in 6 adult mongrel dogs (average weight, 20 kilograms) with 2 survivors. The cause of death in the 4 dogs that died during the operation was acute right heart failure secondary to stenosis of the orifice of the transposed left pulmonary artery. Both of the dogs that survived operation were studied postoperatively by right heart catheterization and angiocardiography, one at 6 and 13 months and the other at 9 months after operation.

RESULTS

Right heart catheterization in both dogs at the postoperative intervals mentioned above revealed a peak systolic pressure in the right ventricle of about 40 mm. Hg. The angiocardiographic studies revealed no evidence of aneurysm

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From the Department of Surgery, The Children's Medical Center, and the Harvard Medical School.

This research was aided by grants from the National Heart Institute, National Institutes of Health, U. S. Public Health Service, and from the American Heart Association.

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formation or of significant contracture in either graft (Figs. 2 and 3). One of the 2 dogs that survived operation died at 17 months after operation, while the other dog is in good condition at 16 months after operation. The dog that died developed moderate ascites at 12 months but remained active up to the day of death. The repeat studies of this dog at 13 months (Fig. 3) did not substantiate our clinical impression that the ascites was secondary to contracture of the graft. Autopsy examination revealed moderate ascites, hepatic congestion, an enlarged right atrium and right ventricle, tricuspid insufficiency, and slight narrowing

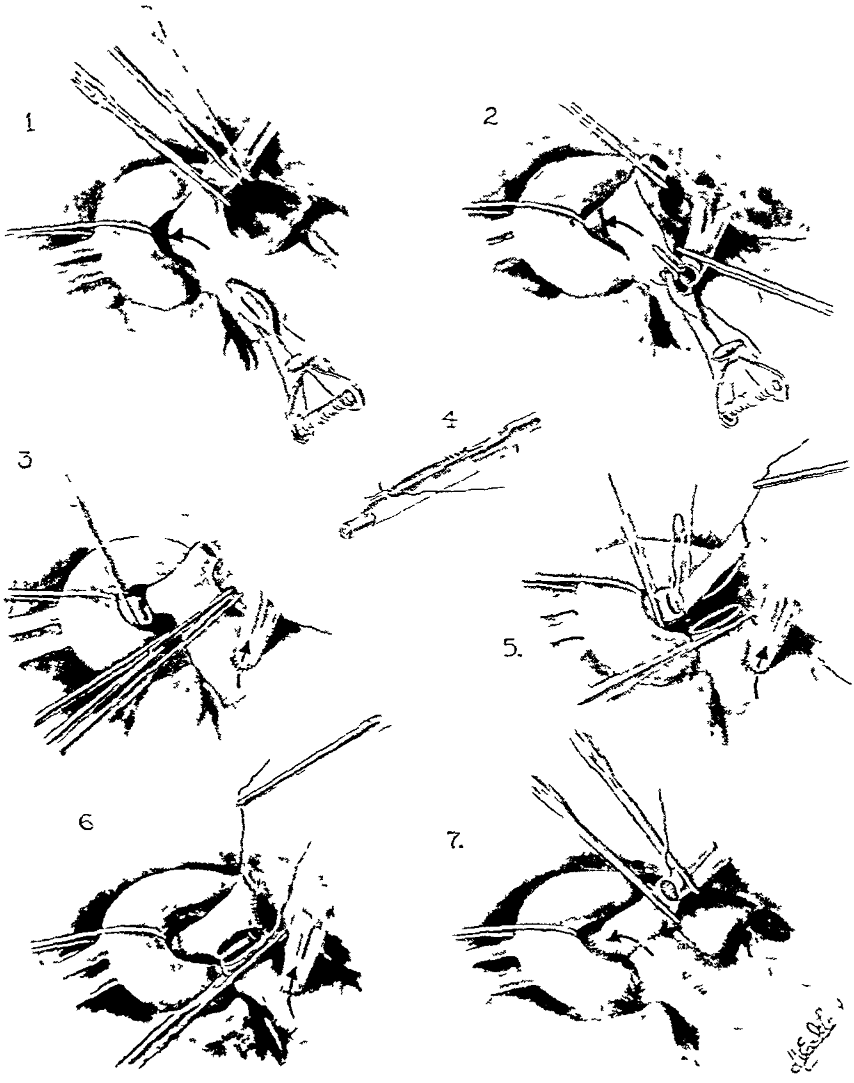

Fig 1.—Technique for the experimental resection and replacement of the distal main pulmonary artery, its bifurcation, and the major portions of both right and left pulmonary arteries by a pericardial autograft.

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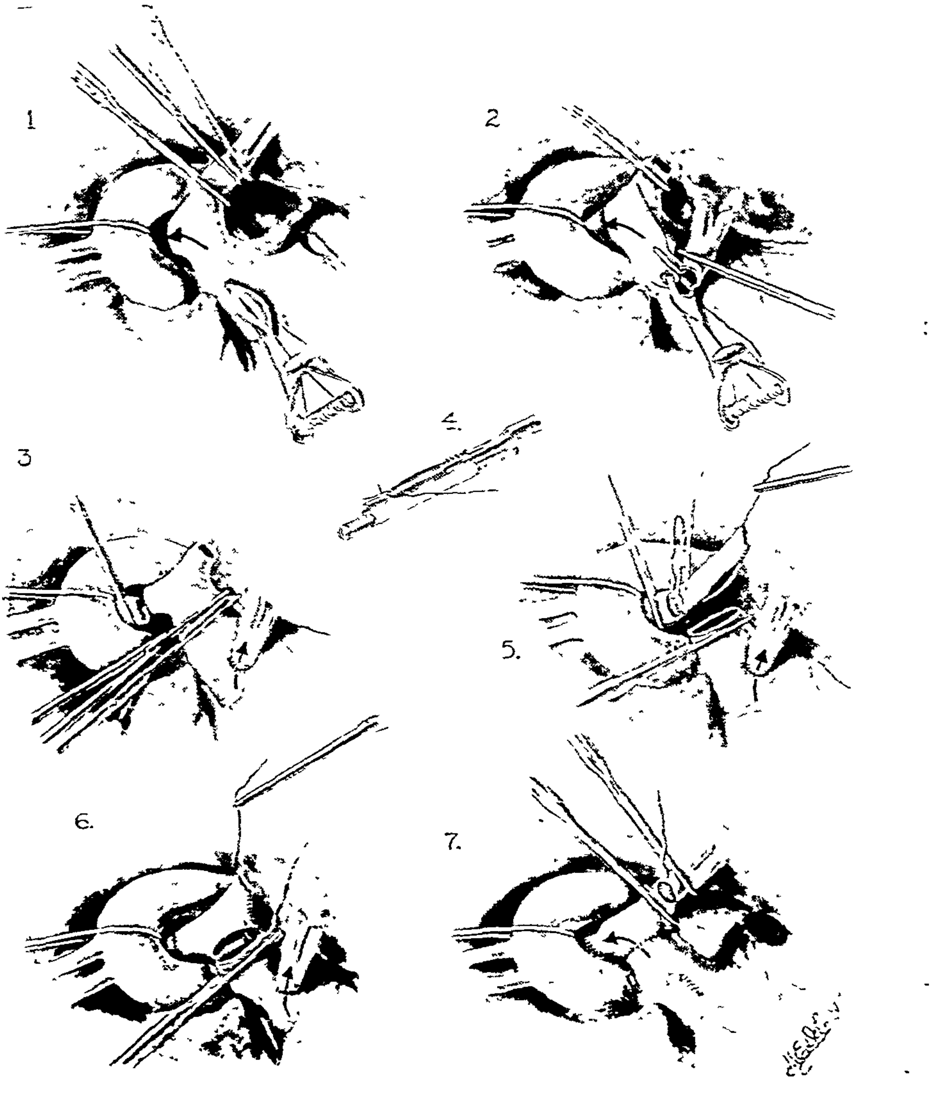

Fig. 1.—Technique for the experimental resection and replacement of the distal main pulmonary artery, its bifurcation, and the major portions of both right and left pulmonary arteries by a pericardial autograft.

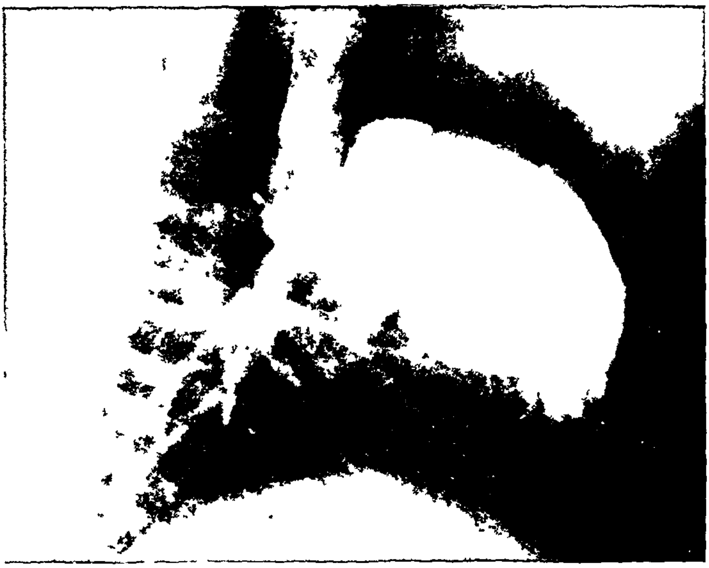

Fig 2—Angiocardiogram made 9 months postoperatively, in right lateral projection of dog with pericardial autograft replacement of the distal main pulmonary artery, its bifurcation, and the major portions of both right and left pulmonary arteries Ninety per cent Hypaque was injected through a catheter positioned in the right external jugular vein Note the opacified superior vena cava, right atrium, right ventricle, and the pulmonary arterial tree There is neither aneurysmal dilatation nor significant contracture of the graft The shadow visible above the right ventricular outflow tract is the normal-sized appendage of the right atrium Right heart catheterization revealed a peak systolic pressure of 40 mm Hg in the right ventricle and a gradient across the graft of 20 mm Hg

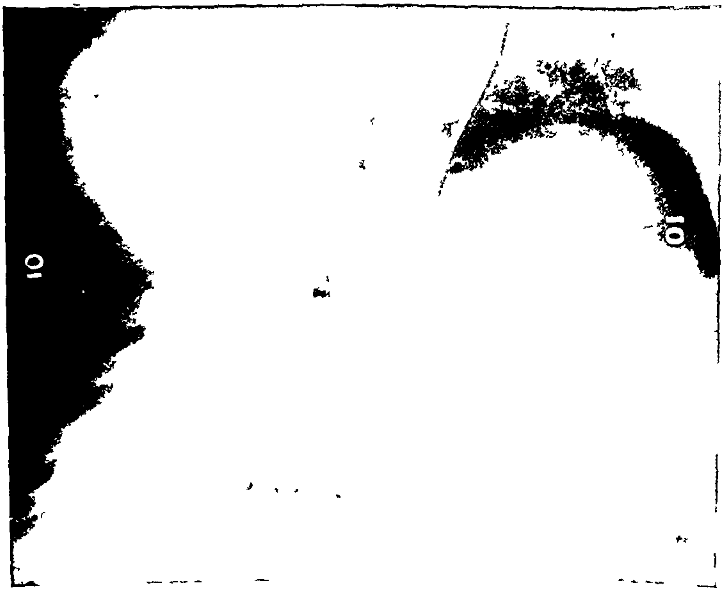

Fig 3—Angiocardiogram made 13 months postoperatively, in right lateral projection, of dog with pericardial autograft replacement of the distal main pulmonary artery, its bifurcation, and the major portions of both right and left pulmonary arteries Ninety per cent Hypaque was injected through the catheter which had been passed from the right external jugular vein down the superior vena cava into the right ventricle Note the absence of aneurysmal dilatation or of significant contracture in the graft. The shadow visible above the right ventricular outflow tract is the enlarged appendage of the right atrium Right heart catheterization revealed a peak systolic pressure of 40 mm Hg in the right ventricle and a gradient across the graft of 20 mm Hg Seven months previously the pressure findings at right heart catheterization were identical However, the angiocardiograms at that time revealed a lesser degree of right atrial enlargement.

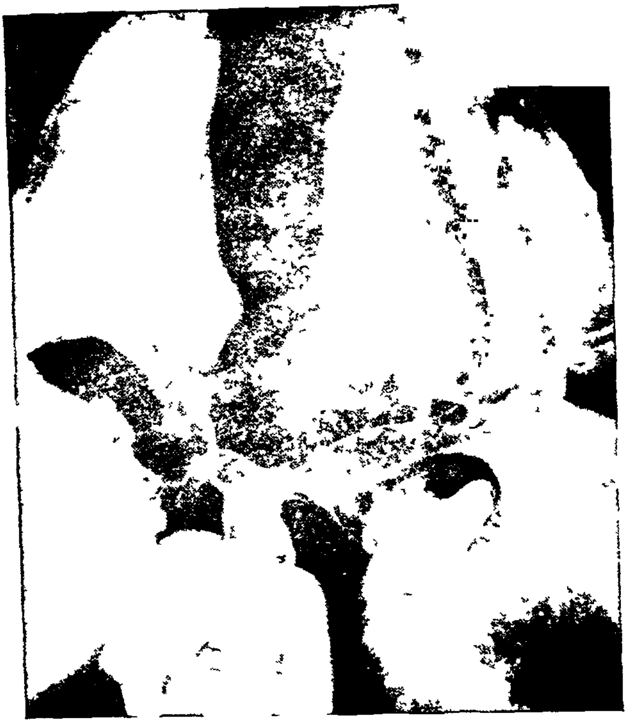

Fig 4.—Roentgenogram, posteroanterior view, of the pulmonary arterial system of the dog dead at 17 months (512 days) after operation. The vessels are inflated to approximately 30 mm. Hg with air via the cannula positioned in the proximal main pulmonary artery. The outflow tract of the right ventricle has been separated from the rest of the heart. The trachea and major bronchi have been excised. The pulmonary veins are ligated at the lobar level. Note the absence of any evidence of calcification. The dimensions of the graft as measured on this roentgenogram are about 25 per cent less than those taken at the time of operation.

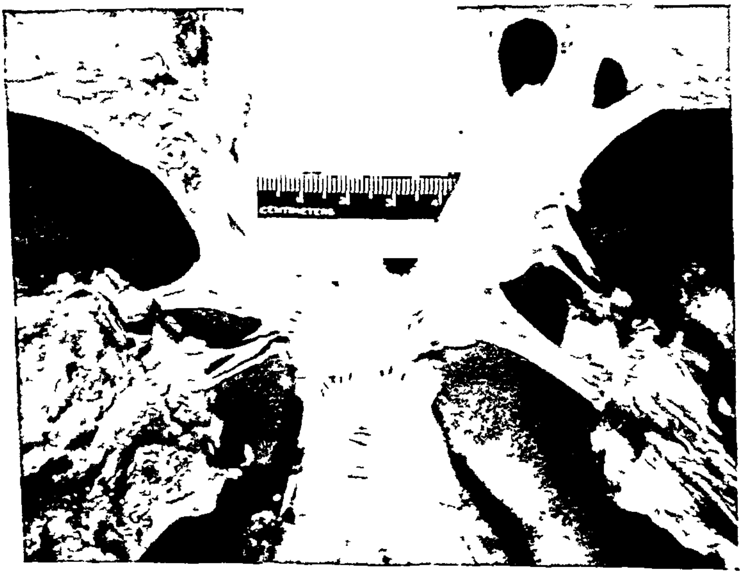

Fig 5.—Photograph of specimen, the roentgenogram of which is seen in Fig 4. This specimen has been opened from the posterior aspect. Note the appearance of the graft. Its inner surface is smooth and glistening. The suture lines are well healed and the walls of the graft are soft and pliable. The vertical suture line in the main pulmonary artery adjacent to the valve is the site where the left pulmonary artery had been anastomosed during implantation of the graft (see Fig 1).

of the graft (Fig. 4). The graft was soft, pliable, and free of degenerative change. Its inner surface was smooth and glistening. The multiple suture lines were well healed (Fig. 5). There was no evidence of pulmonary infarction.

DISCUSSION

The method described in this paper for resection and replacement of the main pulmonary artery bifurcation is technically difficult of accomplishment. However, the technique could be simplified by interposing a temporary graft between the end of the left pulmonary artery and the right ventricle.

We are greatly interested in the fate of autogenous pericardium in the pulmonary arterial circuit. Robinson, Glotzer, Gilbert, and Hurwitt[1] have shown that aortic homografts in the pulmonary artery are subject to severe degenerative change in the pericardial autograft, reported here to be significant at 17 months (Figs. 4 and 5). In other experimental studies in the dog we have observed pericardial autografts to function well and to show no evidence of degenerative change in the intrathoracic inferior vena cava (Sauvage and Gross[2]) and in the right ventricular outflow tract (Sauvage, Gross, Rudolph, Pontius, and Watkins[3]).

On the basis of these observations and those reported here we are employing autogenous pericardium clinically for widening of the right ventricular outflow tract and of the pulmonary artery in instances of infundibular stenosis or hypoplasia of the artery. Longer periods of observation are required to ascertain the ultimate fate of autogenous pericardium in the pulmonary artery. We are keeping the remaining animal reported in this paper for such purpose.

SUMMARY

A technique for the experimental resection and replacement of the distal main pulmonary artery, its bifurcation, and the major portions of both right and left pulmonary arteries by autogenous pericardium has been presented. We believe this technique of graft implantation to be a useful experimental method, and the satisfactory function of two such pericardial autografts over implantation periods of 16 and 17 months, respectively, to be of clinical significance.

REFERENCES

1. Robinson, G., Glotzer, P., Gilbert, M., and Hurwitt, E. S.: Aortic Homograft Replacement of the Main Pulmonary Artery, J. THORACIC SURG. 36: 555-562, 1958.
2. Sauvage, L. R., and Gross, R. E.: Observations of Experimental Grafts in the Intrathoracic Venae Cavae: A Study of Composite Venous Autografts, Pericardial Autografts, and Ascending Aorta Homografts. (In press.)
3. Sauvage, L. R., Gross, R. E., Rudolph, A. M., Pontius, R. G., and Watkins, E., Jr.: An Experimental Study of Tissue and Prosthetic Grafts With Selected Application to Clinical Intracardiac Surgery. (In press.)

EXPERIMENTAL REPLACEMENT OF THE AORTIC ARCH BY HOMOGRAFTS

Lester R. Sauvage, M.D., Abraham M. Rudolph, M.D., and*
Robert E. Gross, M.D., Boston, Mass.

THIS PAPER has the following three purposes: first, to outline a simplified method for the experimental replacement of the aortic arch and its branches; second, to describe the function over the first year of two homografts so implanted as aortic arch replacements; and third, to present observations of the responsiveness of the cardiovascular system to various stimuli after replacement of the aortic arch.

EXPERIMENTAL METHOD

Six adult mongrel dogs were employed in this study. Each dog was given 30 mg. of sodium pentobarbital per kilogram of body weight intravenously. Hypothermia was induced by partial immersion of the anesthetized animal in cold running tap water for from 10 to 20 minutes (Sauvage, Pontius, Watkins, and Gross[3]). After opening the left hemithorax through the fourth intercostal space, the aortic arch was resected and continuity re-established with an arch homograft by the method depicted in Fig. 1. The key step in this method is that shown in step *3* in which the azygos vein is allowed to drain into the heart while the venae cavae are occluded. Thus, while aortic continuity is interrupted, the coronary circulation is maintained by the azygos inflow into the heart. After occluding the venae cavae, the heart should be allowed to contract several times before the ascending aorta is clamped in order to avoid the development of excessive intracardiac pressures.

Postoperatively, the 2 surviving animals were observed carefully and each was studied by aortography, 1 at 164 days and the other at 178 days after operation. The response of the blood pressure and heart rate to epinephrine, norepinephrine, serotonin, atropine, anoxia, and hypercarbia were determined in 1 of these 2 dogs at 214 days after operation.

RESULTS

Four of the 6 dogs undergoing the procedure illustrated in Fig. 1 died because of problems related either to the technique of implantation or to the

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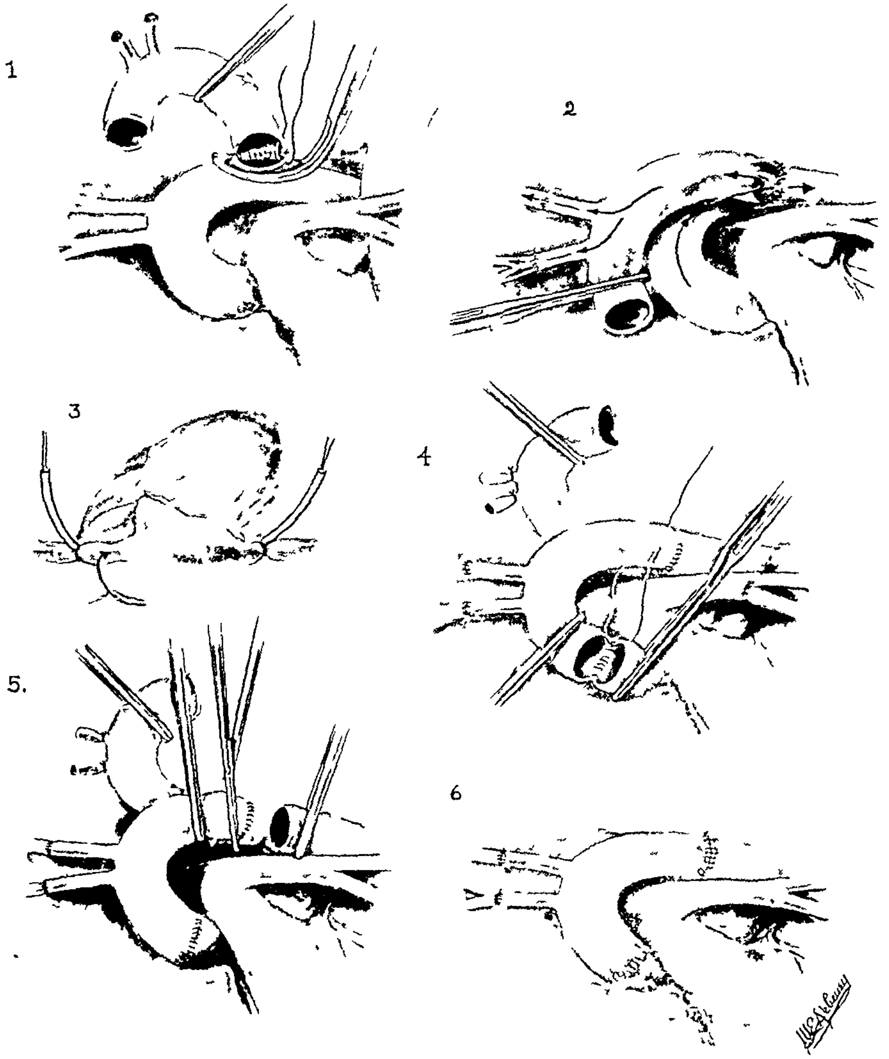

Fig 1 —Method of resecting the aortic arch and restoring continuity by means of an aortic arch homograft. The graft is first anastomosed to the side of the descending thoracic aorta as shown in step *1* Then the left brachial artery (subclavian) of the dog is divided and its distal end anastomosed to the brachial artery branch of the graft The graft is then occluded between the origins of its left brachial and brachiocephal [illegible] The clamps are then removed from the brachial artery and the aorta o [illegible] -established circulation through the left brachial artery by means of a [illegible] shunt A similar procedure is then performed for the anastomosis of th [illegible] tery to the graft. The completed anastomoses for these two branches are shown in step *2* In step *3* the venae cavae are occluded while the azygos vein is left open The heart is allowed to contract several times to deplete the cardiopulmonary circuit of blood before the ascending aorta is clamped The anastomoses of the graft to the ascending aorta is shown in step *4* The coronary circulation is maintained throughout this step by virtue of the azygos vein which was left open in step *3* Following completion of step *4*, the end-to side anastomosis of the graft to the descending aorta is taken down (step *5*) and an end-to-end union effected (step *6*).

development of deep hypothermia. Both of these complications are easily avoidable as experience is acquired with the method. Neither of the 2 dogs that survived this procedure received intravenous fluids or blood transfusions. Both of these animals were rendered moderately hypothermic by immersion in cold running tap water according to the method referred to above.

The first surviving dog, a 16 kilogram animal, after 15 minutes in running tap water at 12° C. had a rectal temperature of 30° C. At the end of operation, the rectal temperature was 28° C. The ascending aorta was occluded for 12 minutes while the graft was anastomosed to the proximal end of the ascending aorta (step *4*, Fig. 1). The heart did not miss a beat during this period of occlusion of the ascending aorta; its contractions remained vigorous throughout and its color pink. This animal recovered normally and manifested no evidence of neurologic damage. The aortogram of this dog at 178 days after operation is shown in Fig. 2. The blood pressure and heart rate responses of this animal to epinephrine, norepinephrine, serotonin, atropine, anoxia, and hypercarbia were studied at 214 days postoperatively and found to be normal. This animal continues to be in excellent general condition at 14 months after operation.

The second surviving animal, an 11 kilogram dog, after 10 minutes in running tap water at 10° C. had a rectal temperature of 32° C. At the end of operation, the rectal temperature was 25° C. The ascending aorta was occluded for 7 minutes while the graft was anastomosed to the proximal end of the ascending aorta (step *4*, Fig. 1). The heart beat strongly throughout the period of occlusion of the ascending aorta, but fibrillation ensued shortly after removal of the occluding clamp as the heart was being displaced from its normal position to allow for removal of blood from the pericardial cavity. However, defibrillation was easily accomplished by one countershock. This animal recovered normally and manifested no evidence of neurologic damage. The aortogram at 164 days after operation is shown in Fig. 3. This animal is now 13 months postoperative and continues to be in excellent general condition.

DISCUSSION

Sauvage and Wesolowski[4] observed that Orlon prostheses were unsuited for use as aortic arch replacements because of kinking in regions of angulation. These grafts were implanted in normothermic animals using a technique that employed retrograde endograft shunts (steps *1* and *2*, Fig. 1) and a shunt from the left ventricle into a side arm of the graft while the prosthesis was anastomosed to the proximal end of the ascending aorta. Satinsky, Neptune, and Alai[5] reported an impressive series of successful homologous transplants of the aortic arch in dogs employing a similar technique. However, the method reported here has seemed easier to perform and, therefore, would appear to have merit as a procedure for laboratory use.

The many complexities of the architecture of the aortic arch have stymied the manufacture of a prosthesis suitable for replacement of this portion of the aorta. It seems probable that aortic arch homografts will continue to be the

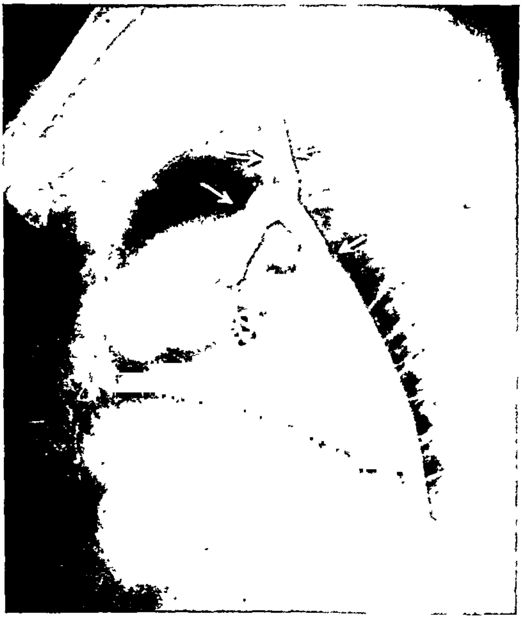

Fig. 2.—Aortogram made 178 days after operation which shows the aortic arch homograft to be functioning satisfactorily. The anastomoses are indicated by arrows. (This graft had been preserved 5 days in saline solution at 4° C. prior to implantation.)

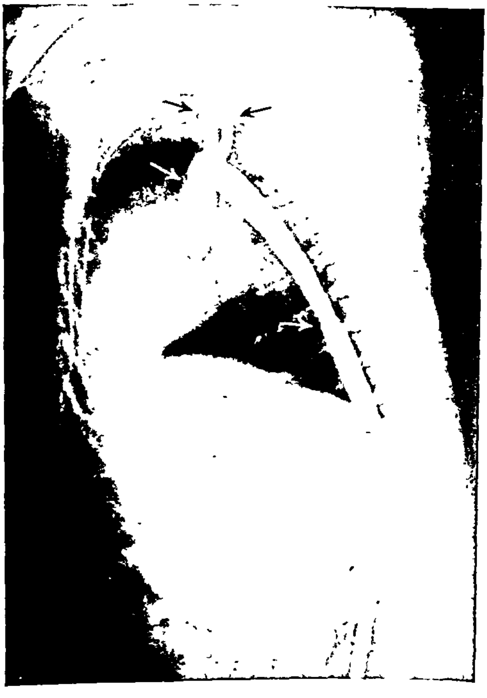

Fig. 3.—Aortogram made 164 days after operation which shows the aortic arch homograft to be functioning satisfactorily. The anastomoses are indicated by arrows. (The graft was 1 hour old at time of implantation.)

preferable type of graft in this location for many years. De Bakey, Crawford, Cooley, and Morris[1] reported the use of a homograft for the first successful clinical replacement of the aortic arch. Extracorporeal circulation was employed to maintain essential blood flow during the period of interruption of aortic continuity. However, little is known of the long-term fate of homografts employed for replacement of the aortic arch. The 2 dogs reported in this paper are being kept for such study and will be reported subsequently.

It is of interest that the response of the cardiovascular system to epinephrine, norepinephrine, serotonin, atropine, anoxia, and hypercarbia was normal in the 1 dog so studied at 214 days after aortic arch resection and homograft replacement. The aortogram of this animal is shown in Fig. 2. It is probable that carotid sinus mechanisms were able to compensate for the loss of the pressor and chemoreceptor mechanisms contained in the aortic arch. Whether similar compensation occurs in the human being is not known.

SUMMARY

An experimental method has been described for replacing the aortic arch that employs retrograde endograft shunts and moderate hypothermia in which cardiac ischemia is avoided by leaving the azygos vein open during the period of vena caval inflow stasis. This technique is recommended for the laboratory study of aortic arch grafts because of its comparative simplicity.

Aortograms at 6 months after operation and clinical observation for 1 year of the 2 dogs in this study indicate excellent function during this implantation period of the homografts employed as aortic arch replacements.

Studies were conducted in 1 of these 2 animals of the responsiveness of the cardiovascular system to a variety of stimuli. The results indicate that replacement of the aortic arch in the dog is not associated with any significant change in cardiovascular reactivity.

REFERENCES

1. De Bakey, M. E., Crawford, E. S., Cooley, D. A., and Morris, G. C., Jr.: Successful Resection of Fusiform Aneurysm of Aortic Arch With Replacement by Homograft, Surg. Gynec. & Obst. 105: 657-664, 1957.
2. Satinsky, V. P., Neptune, W. B., and Alai, J.: Experimental Transplantation of the Complete Arch of the Aorta, Ann. Surg. 141: 38-46, 1955.
3. Sauvage, L. R., Pontius, R. G., Watkins, E., Jr., and Gross, R. E.: A Simple Technique for the Implantation of Experimental Grafts in the Outflow Tract of the Right Ventricle With a Note on Defibrillation of the Hypothermic Canine Heart, Ann. Surg. (In press.)
4. Sauvage, L. R., and Wesolowski, S. A.: The Healing and Fate of Arterial Grafts, Surgery 38: 1090-1131, 1955.

SOME HELPFUL INSTRUMENTS FOR CARDIOVASCULAR SURGERY

Albert Welberry, Ph.D., Elliott Senderoff, M.D., Isadore Kreel, M.D., and Ivan D. Baronofsky, M.D., New York, N. Y.*

I. ATRIAL CLAMP WHICH ALLOWS FOR REPEATED RE-ENTERING OF ATRIUM

ADVANCES in open-heart surgery have necessitated the creation of new instruments designed to meet the special requirements of this field. The clamp shown in Fig. 1 is designed to allow for extensive surgery within the atrial cavity by providing maximum exposure with complete control of the wound. The clamp allows the surgeon to stop at any point in the operative procedure and easily and hemostatically approximate the wound edges by simply approximating the jaws of the clamp. This enables the operator to open and close the atrium and to enter and re-enter the heart as frequently as he desires. In cases performed under complete occlusion of the cardiac inflow, the clamp is of value in extending the operating time by allowing the surgeon to close the atrium, allow a temporary period of cardiac inflow, and then re-enter the atrial cavity to continue the procedure under inflow occlusion. The surgeon is able also to suture the atriotomy wound leisurely in a dry field with no tension on the sutures, as the wound edges are approximated by the clamp when this procedure is performed.

The instrument is a conventional cardiovascular clamp with atraumatic blades. On the outer surface of each blade are three small cross-bars. On the handle is a ratchet which prevents accidental opening of the clamp. There is also a second ratchet which allows the blades to be fixed in the open position. The latter ratchet is controlled by a side bar which can be easily manipulated by the finger. To use this instrument, two parallel rows of guide sutures are placed along the anterolateral wall of the atrium along the line of the projected atriotomy. Each row should contain three sutures. All the sutures are then elevated and the sutures and intervening atrial tissue clamped. The sutures are then tied snugly to the small cross-bars on the outside of the clamp, and the atriotomy made between the two rows of sutures (Fig. 2, *A*).

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The clamp is then opened widely and locked in the open position with the side bar (Fig. 2, *B*). This presents a large rectangular opening in the atrium with excellent exposure of all parts of the atrial chamber. If further exposure is needed, the atriotomy is extended. At the completion of the procedure, air is flushed out of the atrial cavity and the atriotomy rapidly sealed by approximating the clamp blades. If the atriotomy has been extended, the end of the incision is brought between the blades by elevating it with a forceps. The atriotomy may then be subsequently sutured at leisure (Fig. 2, *C*).

The clamp described has had extensive trial in the experimental direct vision production of interatrial septal defects and has been very satisfactory.

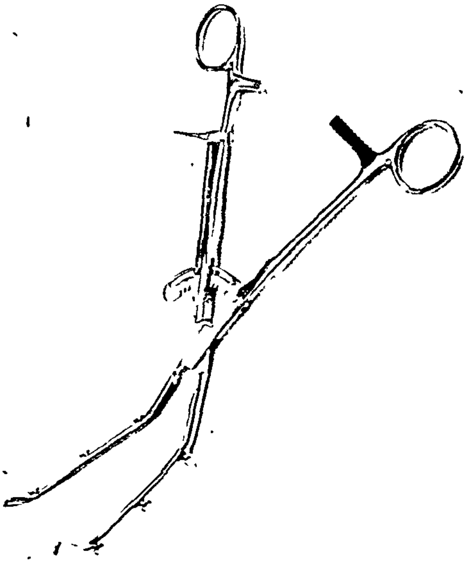

Fig. 1.—Atriotomy clamp.

It is projected for clinical use in the open repair of such defects. The clamp has also been successfully used in the surgical creation of complete heart block in 5 dogs[1] utilizing complete occlusion of the cardiac inflow without hypothermia or cardiac bypass. The clamp permitted repeated entry into the atrial cavity until a ligature effectively producing complete heart block was placed.

The clamp can be made in two angles. The one shown (Fig. 1) is more effective in dog experimentation because of the shallow thoracic cavity. A more acute angle is necessary for the deeper chest of the human being.

II. SUCTION TIP FOR LARGE AND SMALL BLOOD LOSS

The need for adequate suction to maintain a clean operative field is of extreme importance in intracardiac surgery. This is often difficult to achieve despite the varied types of suction units presently available. The unit shown in Fig. 3, *A* has been designed to provide effective and efficient suction of both

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The clamp is then opened widely and locked in the open position with the side bar (Fig. 2, *B*). This presents a large rectangular opening in the atrium with excellent exposure of all parts of the atrial chamber. If further exposure is needed, the atriotomy is extended. At the completion of the procedure, air is flushed out of the atrial cavity and the atriotomy rapidly sealed by approximating the clamp blades. If the atriotomy has been extended, the end of the incision is brought between the blades by elevating it with a forceps. The atriotomy may then be subsequently sutured at leisure (Fig. 2, *C*).

The clamp described has had extensive trial in the experimental direct vision production of interatrial septal defects and has been very satisfactory.

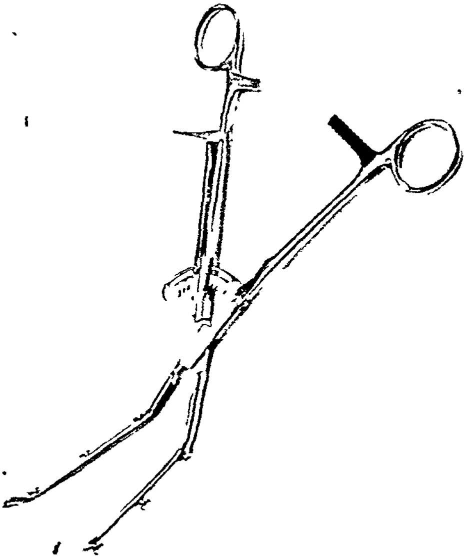

Fig 1.—Atriotomy clamp

It is projected for clinical use in the open repair of such defects. The clamp has also been successfully used in the surgical creation of complete heart block in 5 dogs[1] utilizing complete occlusion of the cardiac inflow without hypothermia or cardiac bypass. The clamp permitted repeated entry into the atrial cavity until a ligature effectively producing complete heart block was placed.

The clamp can be made in two angles. The one shown (Fig. 1) is more effective in dog experimentation because of the shallow thoracic cavity. A more acute angle is necessary for the deeper chest of the human being.

II. SUCTION TIP FOR LARGE AND SMALL BLOOD LOSS

The need for adequate suction to maintain a clean operative field is of extreme importance in intracardiac surgery. This is often difficult to achieve despite the varied types of suction units presently available. The unit shown in Fig. 3, *A* has been designed to provide effective and efficient suction of both large and small amounts of fluid. The unit is available in three sizes with internal diameters ranging from 3 to 6 mm. Despite this large inflow capacity, the design is such that the suction tip is not bulky and cumbersome. The instrument shown disassembled (Fig. 3, *B*) consists of an inner tubular shaft, an outer shaft, a tip consisting of four lateral holes and one distal hole, a spring controlled lever, and a handle. In the resting position (Fig. 4, *A* and *B*), all the inlet orifices are open and large amounts of fluid (1,150 to 2,400 c.c. per minute, depending upon size of suction unit) can be easily handled. This unit is also capable of handling the remaining small pools and drops of blood which tend to obscure the operative field. In most suction units, when an attempt is made to remove a small pool or drop of fluid, air enters the inlets before the fluid does. This breaks the effective vacuum and the suction tip does not function. In the unit described, upon depressing the lever, the side inlets are shut off (Fig. 4, *C*) and only the distal orifice of the suction tip is operative. This allows the

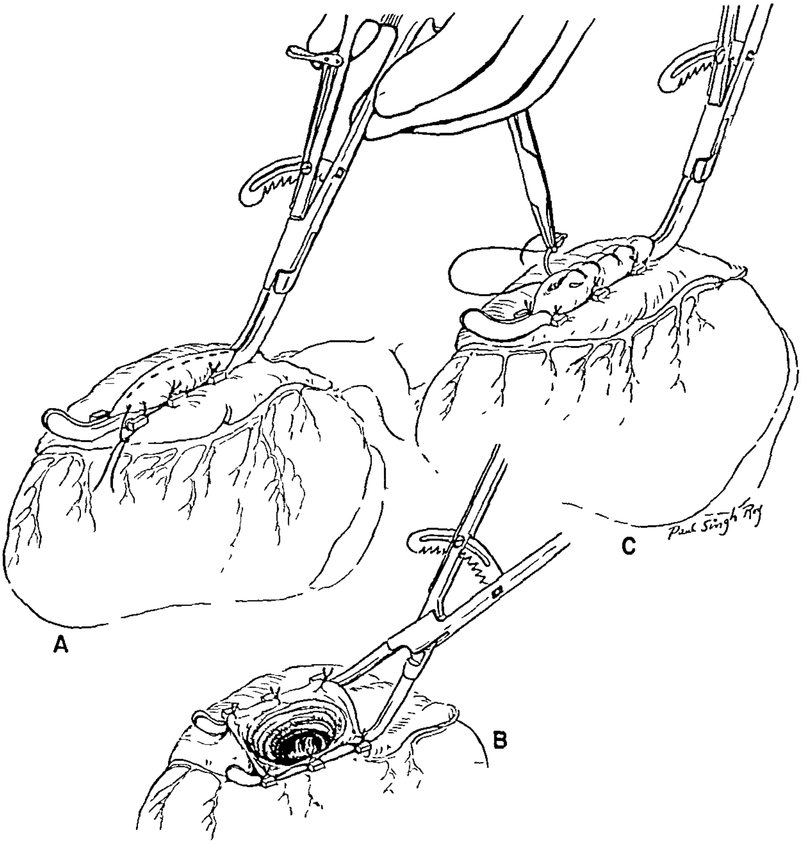

Fig. 2.—*A*, Atriotomy clamp in position on wall of atrium. Note sutures tied about the cross-bars of the clamp securing the atrial wall to the clamp blades. Dotted line indicates line of proposed incision in the tissue between the clamp blades.

B, Clamp locked in the open position. The wound edges and the extent of the wound opening are completely controlled by the clamp blades.

C, Clamp closed at the end of the operative procedure. The atriotomy incision can be sutured at leisure in a dry field.

suction to be concentrated at the end of the tip only. In this manner the smallest drop of fluid can be removed from the field. When flooding occurs, the lever is released, the spring forces the handle up and the suction unit is once again able to handle large quantities of fluid. When dealing with small amounts of blood, this unit also decreases turbulence of the stream and the subsequent hemolysis of red blood cells as air is not able to mix with the blood when the lever is depressed. Since the suctioned blood is recirculated in cardiac bypass operations, it is important and advantageous to have a minimum of hemolysis occur as a result of the suction unit employed.

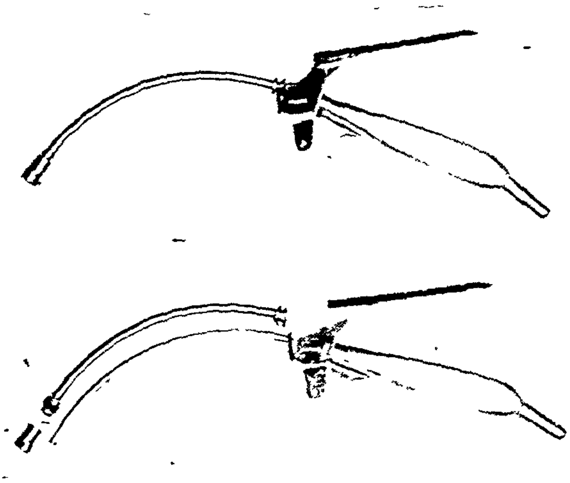

Fig. 3.—Suction unit. *B*, Suction unit disassembled.

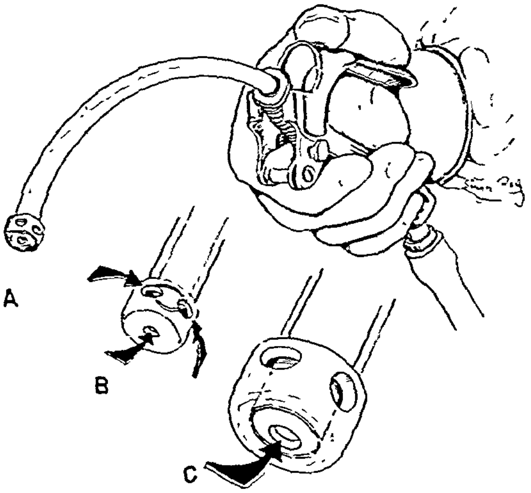

Fig. 4.—*A*, Suction unit.
B, Drawing of tip of suction unit showing side and distal inlet orifices operative in the usual resting position of the inner shaft.
C, Drawing of tip of suction unit when lever on handle is depressed. Inner shaft has been advanced to meet the distal orifice. This closes the side inlets and causes the suction to be operative at the distal orifice only.

SUMMARY

Two new instruments* for use in the field of intracardiac surgery have been presented. A clamp for easy and effective control of atriotomy incisions and a suction unit capable of handling fluid volumes ranging from minute to large amounts with a minimum of hemolysis have been described.

REFERENCE

1. Kahn, M., Senderoff, E., Shapiro, J., Bleifer, S., and Grishman, A.: Bridging of Interrupted A-V Conduction in Experimental Chronic Heart Block by Electronic Means Am. Heart J. 59: 548, 1960.

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*The instruments described are manufactured by Edward Weck & Co., Inc., 135 Johnson Street, Brooklyn 1, N. Y.

BRONCHIECTASIS: RESULTS OF PULMONARY RESECTION

Lieutenant Colonel Thomas H. Hewlett, MC, USA, Fort Sam Houston, Texas, and Lieutenant Colonel H. Haskell Ziperman, MC, USA,** San Francisco, Calif.*

THE FREQUENCY of bronchiectasis has been emphasized in reports originating from hospitals which are devoted primarily to the management of pulmonary disease. The true incidence of this disease in the general population has not been clarified. Proved bronchiectasis is a surgical problem from the standpoint of either palliation or cure, and a significant period of time is devoted to the diagnostic investigation of suspect patients. Evaluation of the problem as it exists in the population served by a general hospital could be expected to clarify the incidence of the disease, as well as to confirm the results of surgical treatment.

The period 1949 to 1958 was chosen for study. All proved cases of bronchiectasis studied or treated by the Thoracic Surgical Service of Brooke Army Hospital are herein reported.

The yearly summary reports were utilized in deriving average figures in several categories. Excluded from the admission figures are (1) births, and (2) patients with proved diagnosis of active pulmonary tuberculosis.

TABLE I. ADMISSIONS

HOSPITAL ADMISSIONS	PATIENTS WITH PULMONARY DISEASE	CLINICALLY DIAGNOSED AS BRONCHIECTASIS	BRONCHOGRAPHY PERFORMED	PROVED BRONCHIECTASIS
20,792	560	61	85	11.5
Incidence of Bronchiectasis				
per 1,000 admissions			0.55	
per 100 patients with pulmonary disease			2.05	
per 100 bronchograms			13.5	

The existence of bronchiectasis is proved bronchographically in 1 out of every 6 suspects. It is immediately apparent that the majority of the patients subjected to diagnostic study because of chronic cough do not have bronchiectasis. Bronchoscopy in these patients discloses chronic changes in the bronchial mucosa. Bronchograms fail to reveal bronchiectatic changes. A diagnosis of chronic bronchitis has been applied to such patients, such a diagnosis being arrived at by elimination. Compared with the incidence of other

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chronic pulmonary diseases, bronchiectasis has become a relative rarity thereby confirming the prediction that this disease entity would decrease in frequency as a direct result of more efficient management of acute respiratory infection in children and adults. More effective treatment has evolved concomitantly with the development of broad spectrum antibiotics.

CLINICAL MATERIAL

One hundred and fifteen consecutive proved cases of bronchiectasis were studied. The disease was unilateral in 95 patients and bilateral in 20 patients. One hundred and seven patients were treated by pulmonary resection—103 unilateral resections and 4 bilateral resections, totaling 111 operations. Eight of the 115 patients were not treated surgically. Eighty-two or 76.6 per cent were male; 33 or 23.4 per cent were female. There were only 5 Negro adults in the group. Six children are included in the series.

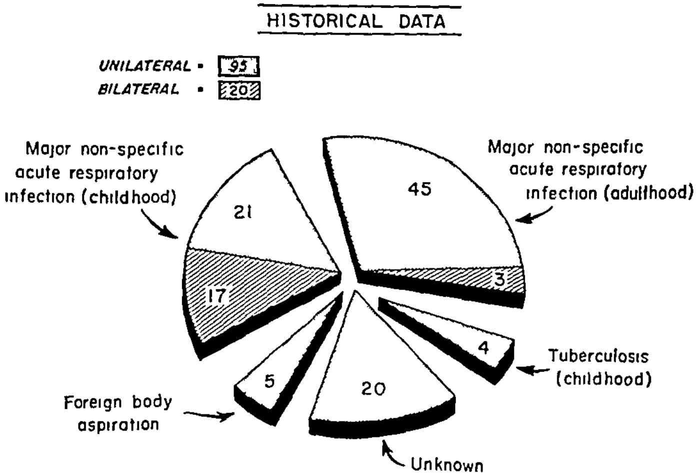
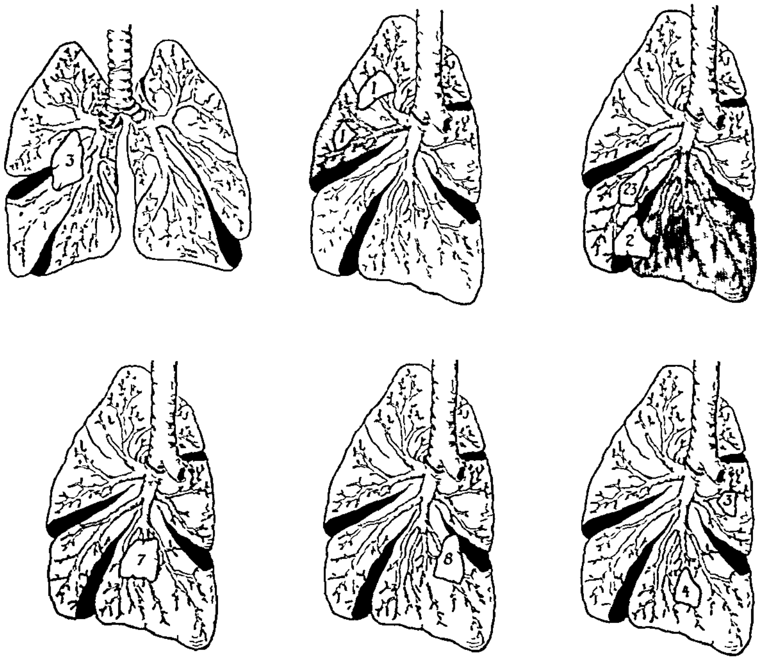


Fig. 1

The symptomatology was consistent with that recorded in numerous reports and merits no repetition. Significant sputum volumes were recorded only in patients with severe bilateral disease. The ages range from 2 to 63, with an average age of 28. The average duration of symptoms was 6 years.

In 82.6 per cent of the patients studied, a positive significant history could be obtained. The childhood origin of the disease was consistently emphasized by repeated bouts of moderate upper respiratory infection during the winter months which tended to limit the school attendance. Since the report of Ochsner and associates[9] in 1949, little attention has been paid to the medical history of these patients. The fact that only 33 per cent of the patients studied were able to trace the origin of their disease to childhood suggests that the majority of cases no longer develop during childhood.

Of the patients studied, 41.7 per cent traced the onset of their bronchiectasis to a documented major respiratory infection in adulthood. This is significant as it establishes the fact that bronchiectasis can and does develop in the adult. Three of the patients studied had bronchograms carried out early during their convalescence from atypical viral pneumonia. The initial films revealed bilateral basilar pseudo-bronchiectasis. Within a 6-month period, during which repeated bronchography was performed, bronchiectatic changes disappeared on one side and become permanent on the other. Resected specimens in each instance revealed the permanent pathologic changes of cylindrical bronchiectasis. It has been observed that the pseudo-bronchiectasis, which follows atypical pneumonia in the young adult, will clear usually within 90 days following the disappearance of acute symptoms. Aggressive therapy of acute pneumonic processes in the adult must include adequate attention to airway toilet if the development of irreversible bronchiectasis is to be prevented.



RIGHT PULMONARY RESECTIONS - TOTAL 52

Fig. 2.

The physician treating acute respiratory infections in the adult should be reminded of the statement by Gross[6]: "Bronchiectasis rises slowly out of the smoldering ashes of some previous pulmonary insult or long continued pulmonary inflammation."

PULMONARY RESECTIONS

Unilateral disease is almost equally distributed between the two lungs with the marked predilection for the lower lobes. Bilateral disease was present in 20 or 17.3 per cent of the patients studied. Of these, 60 per cent were treated with unilateral resection; 20 per cent had bilateral resections.

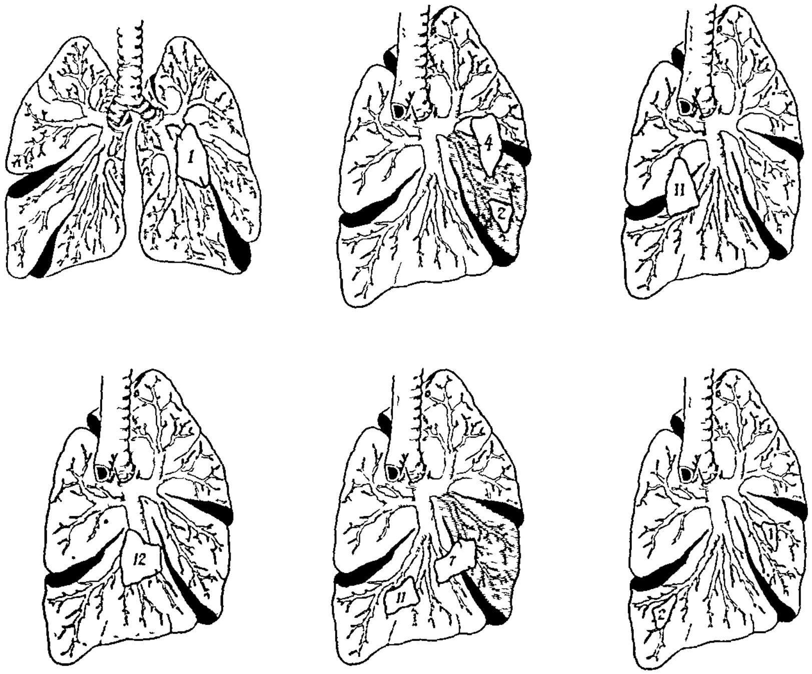

LEFT PULMONARY RESECTIONS - TOTAL 51

Fig. 3.

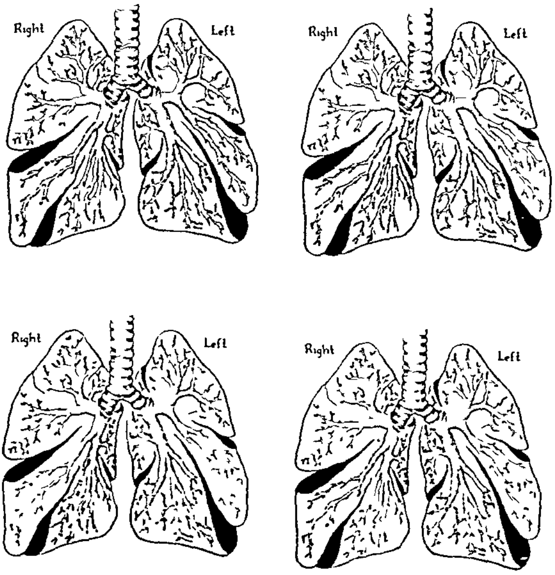

STAGED BILATERAL PULMONARY RESECTIONS - TOTAL 8

Fig. 4.

Eight patients in the series received no surgical treatment. Four had severe bilateral disease with critical maximum breathing capacities. Three with unilateral disease refused treatment. One patient had severe contralateral residual disease following previous lobectomy in another institution. There are no pulmonary cripples as a result of bilateral resection; the 4 patients enjoy reasonable health and are fully active.

In all operations, hilar dissection has been used with individual ligation of the vessels and closure of the bronchial stump with interrupted nonabsorbable sutures. In lower lobe resections it has been routine to preserve the superior segment when possible. This has not resulted in an increase in complications and its economic soundness is attractive. Preoperatively, patients have been carefully instructed in breathing exercises and this exercise is started under supervision the day after operation. Aggressive airway care, consisting of tracheal aspiration and coughing, is started on a 15 to 30 minute routine as soon as the patient reacts from anesthesia. Water seal drainage of the pleural space is maintained for at least 18 hours and longer if complications occur. Pleural space suction was used only when a bronchopleural fistula developed. Penicillin and streptomycin have been administered for 7 days postoperatively. Preoperative antibiotics have been used only in bilateral disease.

COMPLICATIONS

A total complication rate of 19.8 per cent is considered high but not unreasonable when it is realized that 70 per cent of the operations were performed by residents in their third and fourth years of general surgical training. In view of complication rates of 25.8 per cent reported by Ginsberg[3] in 1955, one of 22.8 per cent reported by Bradshaw[1] in 1957, and 41.6 per cent reported by Helm[2] in 1958, it appears that a rate in the range of 20 per cent is acceptable with current techniques.

TABLE II. COMPLICATIONS (111 OPERATIONS)

TYPE	NUMBER	TREATMENT	RESULT
Bronchopleural fistula	8	Tube drainage – 7 Thoracoplasty – 1	Cured
Bronchopleural fistula empyema	1	Tube drainage – 1	Cured
Hemothorax	3	Thoracotomy – 3	Cured
Empyema	1	Tube drainage – 1	Cured
Atelectasis	1	Bronchoscopy – 3 times	Cured
Hemoptysis	1	Bronchoscopy, conservative – 1	Cured
Minor wound infection	3	Local	Cured
Major wound infection	1	Secondary closure	Cured

Complication rate – 19.8%

Bronchopleural fistula – 51.5%

75% of bronchopleural fistulas associated with stump of lingula bronchus

As the direct result of constant awareness of the problems resulting from retained secretions, it has been possible to prevent complications directly

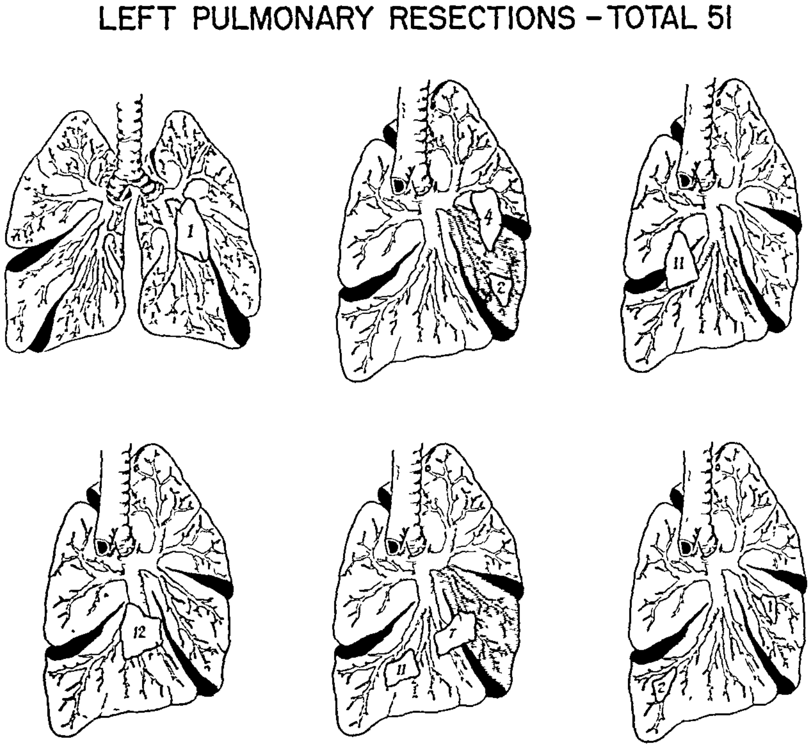

LEFT PULMONARY RESECTIONS - TOTAL 51
1
4
2
11
12
7
11
1
2

Fig. 3.

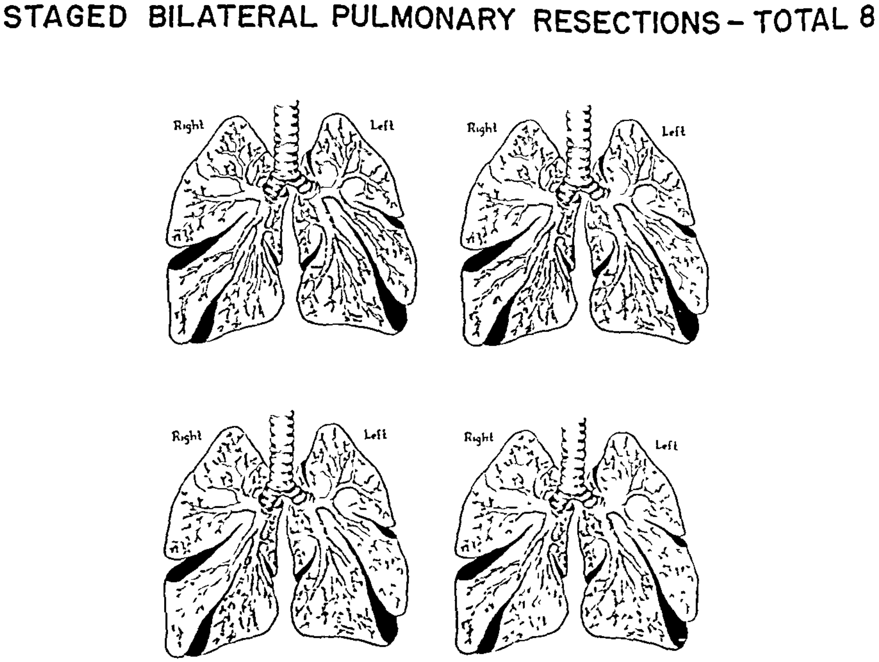

STAGED BILATERAL PULMONARY RESECTIONS - TOTAL 8
Right
Left
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Fig. 4.

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A total complication rate of 19.8 per cent is considered high but not unreasonable when it is realized that 70 per cent of the operations were performed by residents in their third and fourth years of general surgical training. In view of complication rates of 25.8 per cent reported by Ginsberg[5] in 1955, one of 22.8 per cent reported by Bradshaw[1] in 1957, and 41.6 per cent reported by Helm[7] in 1958, it appears that a rate in the range of 20 per cent is acceptable with current techniques.

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Empyema	1	Tube drainage - 1	Cured
Atelectasis	1	Bronchoscopy - 3 times	Cured
Hemoptysis	1	Bronchoscopy, conservative - 1	Cured
Minor wound infection	3	Local	Cured
Major wound infection	1	Secondary closure	Cured

Complication rate — 19.8%
Bronchopleural fistula — 54.5%
75% of bronchopleural fistulas associated with stump of lingula bronchus

As the direct result of constant awareness of the problems resulting from retained secretions, it has been possible to prevent complications directly traceable to this factor. Each patient receives preoperative indoctrination as to the technique and value of coughing. Breathing exercises are taught preoperatively and resumed under supervision on the first postoperative day. Any patient who develops significant secretions during operation is bronchoscoped at the conclusion of operation. Tracheal suction is used on a 15 to 30 minute schedule during the first 48 hours. In the early postoperative period, bronchoscopy is performed if the efficiency of the tracheal suction or cough is questionable. Consequently, the development of atelectasis is rare. Such a program necessitates round the clock attention by the house staff.

Bronchopleural fistula associated with a segmental bronchial stump is a well-recognized hazard and is most likely related to the destruction of bronchial vessels incidental to the resection technique. Complete skeletonization of the segmental bronchus was frequently evident in the operations performed during the first few years of this experience, the period in which the major portion of the complications appeared. The only significant variation in technique has been the adoption of minimal dissection in the region of the origin of the segmental bronchus to produce a bleeding bronchial stump in preference to one which is devoid of peribronchial tissue. Following closure of the bronchial stump, the bleeding is controlled by superficially placed suture ligatures. It is our clinical impression that this has been significant in reducing the instance of bronchopleural fistula. We have not been aware of lung difficulty traceable to operative injury of intersegmental veins.

Intrapleural air pockets which appear following removal of the thoracotomy tubes are considered as diagnostic of fistula and are treated by suction drainage. The early use of tube drainage seems to reduce the incidence of empyema as a concomitant complication of fistula.

Complications have contributed to poor results in 2 of 4 patients not improved by operation. Of the complications listed, 60 per cent occurred during the first 5 years of the experience.

RESULTS

Table III. Results

RESULTS	UNILATERAL DISEASE	BILATERAL DISEASE		FOLLOW-UP PERIOD	PER CENT	BENEFITED
		I	II			
Cured	27	1		3.7 yr.	36.4	94.8%
Improved*	37	4	4	5 yr.	58.4	
None	3	1		3 yr.	5.2	5.2%

*Two late deaths occurred in patients who were improved.

Of 107 patients treated by resection we have follow-up information on 77 or 71.9 per cent; of these 75 are alive. There have been two late deaths not attributable to bronchiectasis.* One patient died of carcinoma in the opposite lung 2 years after operation. One patient died of generalized peritonitis 3 years following lobectomy. Thirty patients have been lost to follow-up.

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*These deaths were in patients who were improved.

"Cured" designates those patients who are free of symptoms and have no limitation of activity; 36.4 per cent of the group fall into this category. The patient with a single operation in bilateral disease has had no progression of mild anatomic changes in the unoperated lung.

"Improved" designates those patients who continue to have a cough but are able to carry out normal physical activity; 58.4 per cent of the group fall into this category. In addition to cough, minor occasional hemoptysis is reported by 5 patients. Increased susceptibility to respiratory infection is reported by 3 patients. Three of the 4 patients undergoing bilateral resection report mild dyspnea on exertion. It should be noted that the residual cough is frequently described as dry in distinction to the characteristic productive cough that existed prior to operation. A significant number of the patients who continue to cough have resumed smoking since operation.

"Poor" is applied to those patients who have not been improved by operation. Marked productive cough continues and their physical activity is limited to the point that they cannot be gainfully employed; 5.2 per cent fall into this category.

Seventy-three patients or 94.8 per cent were benefited by resection and are employed.

Comparison of Results.—A survey of the surgical experience with bronchiectasis published during the period of this study may be used as a basis for predicting results in surgical treatment of the disease. A complication rate of 22.8 per cent can be anticipated; however, the mortality rate should remain less than 1 per cent. An average cure rate of 43.2 per cent is expected while another 42.6 per cent should be improved by operation. Of those patients treated, 85.8 per cent should be benefited and capable of normal activity following operation. Surgical treatment will fail in approximately 6.2 per cent.

TABLE IV. COMPARISON OF RESULTS

AUTHOR	DATE	PATIENTS	% CURED	% IMPROVED	% POOR	% MORTALITY	% BENEFITED
Ochsner et al.[9]	1949	82	44.9	34.4	4.2	0	79.3
Ginsberg et al.[5]	1955	221	75.0	16.0	5.0	0	91.0
Bradshaw et al.[1]	1957	270	21.1	61.5	6.6	0	82.6
Helm and Thompson[7]	1958	159	41.0	43.0	10.0	6	84.0
Brooke Army Hospital	1959	77	36.4	58.4	5.2	0	94.8

DISCUSSION

The aggressive diagnostic approach generally utilized in the evaluation of patients with symptoms of pulmonary disease is essential in the diagnosis and management of bronchiectasis. That bronchiectasis can originate in the adult is becoming well established, a fact which will modify the earlier concept of the disease being one which generally originated during childhood.

Classification of bronchiectasis into primary and secondary types is of didactic interest only. A true bronchial obstructive phenomenon exists in the early phases of the disease. There is no evidence to suggest that the pathologic changes, distal to the site of foreign body bronchial occlusion, differ in any way from those changes which develop distal to bronchial occlusion which is the result of localized edema and infiltration occurring in acute pulmonary infection. The combination of some degree of bronchial obstruction and distal inflammation is constant in the development of bronchiectasis.

The continued reporting of surgical experiences with bronchiectasis confirms the efficacy of resection as both a palliative and curative measure. The advanced saccular type disease appears to be decreasing in frequency, with the advanced cylindrical pattern being noted frequently. This is undoubtedly due to earlier use of bronchography in the evaluation of patients with pulmonary symptoms; thus the bronchial changes are recognized before they progress to marked saccule formation. Pulmonary resection is never recommended solely on the basis of radiographic changes but is reserved for those patients in whom there is an unquestionable history of chronic pulmonary symptoms associated with permanent changes in the bronchographic pattern.

The complication and mortality rates associated with earlier experiences of pulmonary resection for bronchiectasis have constantly decreased with the use of individual dissection and ligation of hilar structures, the general availability of endotracheal anesthesia, alert postoperative care aimed at maintaining a clear airway, and the prevention of infection by the use of antibiotics to counteract pleural contamination incidental to operation.

Pulmonary resection is the treatment of choice in all age groups.

REFERENCES

1. Bradshaw, H. H., Myers, R. T., and Cordell, A. R.: Bronchiectasis: A Fourteen Year Appraisal, Ann. Surg. 145: 644-649, 1957.
2. Brinkman, G. L., and Rauli, H.: The Results of Surgery for Bronchiectasis, Henry Ford Hosp. Med. Bull. 6: 318-322, 1958.
3. Forsee, J. H., and Klinger, P. E.: Lobectomy for Bronchiectasis, Ann. Surg. 137: 74-76, 1953.
4. Ginsberg, R. L.: Prognosis of Bronchiectasis After Surgical Resection, Surg. Gynec. & Obst. 101: 99-102, 1955.
5. Ginsberg, R. L., Cooley, J. C., Olsen, A. M., and Kirklin, J. W.: An Analysis of Unfavorable Results in the Surgical Treatment of Bronchiectasis, J. THORACIC SURG. 30: 331-334, 1955.
6. Gross, R. E.: Bronchiectasis *in* The Surgery of Infancy and Childhood, Philadelphia, 1953, W. B. Saunders Co., pp. 785-805.
7. Helm, W. H., and Thompson, V. C.: The Long Term Results of Resection for Bronchiectasis, Quart. J. Med. 27: 353, 1958.
8. Lindskog, G. E., and Hubbell, D. S.: An Analysis of 215 Cases of Bronchiectasis, Surg. Gynec. & Obst. 100: 643-650, 1955.
9. Ochsner, A., De Bakey, M., and DeCamp, P. T.: Bronchiectasis: Its Curative Treatment by Pulmonary Resection, Surgery 25: 518-532, 1949.

INFLUENZAL PNEUMONIA AND BLOOD GAS ANALYSIS

An Attempt at Correlation Between Anatomic and Functional Findings

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ONE of the striking findings in gas analyses of arterial blood in patients with influenzal pneumonia was a marked reduction of oxygen saturation levels.[1, 2] This fact was advanced to explain the deep cyanosis of the patients.

The cause of this insufficient oxygen saturation may be sought in the following factors: (1) obstruction of alveolar and bronchiolar lumen by secretion, edema fluid, blood, and exudate, (2) impairment of gas diffusion because of thickening of alveolar wall by edema and inflammatory exudate, and (3) hypoventilation caused by pleural pain and possible toxic damage to the respiratory center.

We have been mainly interested in examining the role played by the lung arteries and arterioles in this process. According to von Euler and Liljestrand,[3] inspiration of air poor in oxygen or rich in carbon dioxide results in a rise of pulmonary pressure in the animal. If such arterial contraction would come into play to diminish the blood supply to individual, poorly aerated, lung portions, then—according to these authors—this would be a protective mechanism; among other things, little or no mixing of nonoxygenated blood from alveolar capillaries (e.g., because of diffusion impairment due to alveolar exudate) with blood rich in oxygen from healthy lung portions would occur.

This mechanism would allow blood that originally was to flow into poorly aerated lung areas to be deviated into healthy lung tissue. This would maintain the same level of blood pressure in the pulmonary artery, provided of course that sufficient healthy lung parenchyma were available as reserve.

Animal experiments and investigations in human beings by Motley and his associates,[4] who introduced air with a low oxygen content into one and subsequently both lungs, seem to confirm this point of view, inasmuch as no blood pressure rise in the main pulmonary artery resulted from one-sided respiration.

What are the alterations of blood supply that occur in the lung of influenzal pneumonia? Clinically, it was seen that frequently only a small rise in oxygen

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saturation of arterial blood resulted from oxygen breathing (Herzog[2]), and normal values of 95 to 97 per cent could not be obtained. Three main reasons could account for this: (1) arterioles situated in the pneumonic areas would not contract sufficiently to prevent mixing of blood poor in oxygen with blood rich in oxygen; (2) the pneumonic process was too generalized and there were no reserves of healthy functioning lung parenchyma where oxygenation could take place; and (3) unsatisfactory respiratory movements. Naturally also combinations of the three factors would be possible.

We have tried to find out—by studying the postmortem material in 3 typical cases of influenzal pneumonia and comparing the findings with the results of blood gas analyses—whether or not there was a contraction of arteries in the pneumonic areas. We examined by serial sections the material from pneumonic areas: in Case 1, 68 sections; in Case 2, 24 sections; and, in Case 3, 54 sections. In order to make the arteries stand out better we used, in addition to hematoxylin and eosin stain, Weigert's fuchsin elastic tissue stain.

CASE REPORTS

Case 1.—G. G., a 55-year-old man, had never been seriously ill before. On Oct. 14, 1957, fatigue set in; the following day noisy respiration was noticed. On October 16, the temperature rose to 38.5° C. He was admitted to the hospital on October 18. Loss of weight and dyspnea were apparent; râles were heard over both lung fields, and a friction rub over the right base was present. He was treated with penicillin, erythromycin, streptomycin, hydrocortisone, blood transfusions, and oxygen therapy. On October 19 (the sixth day of illness and 2 days before death), blood gas determination of arterial blood was performed [italics are ours].

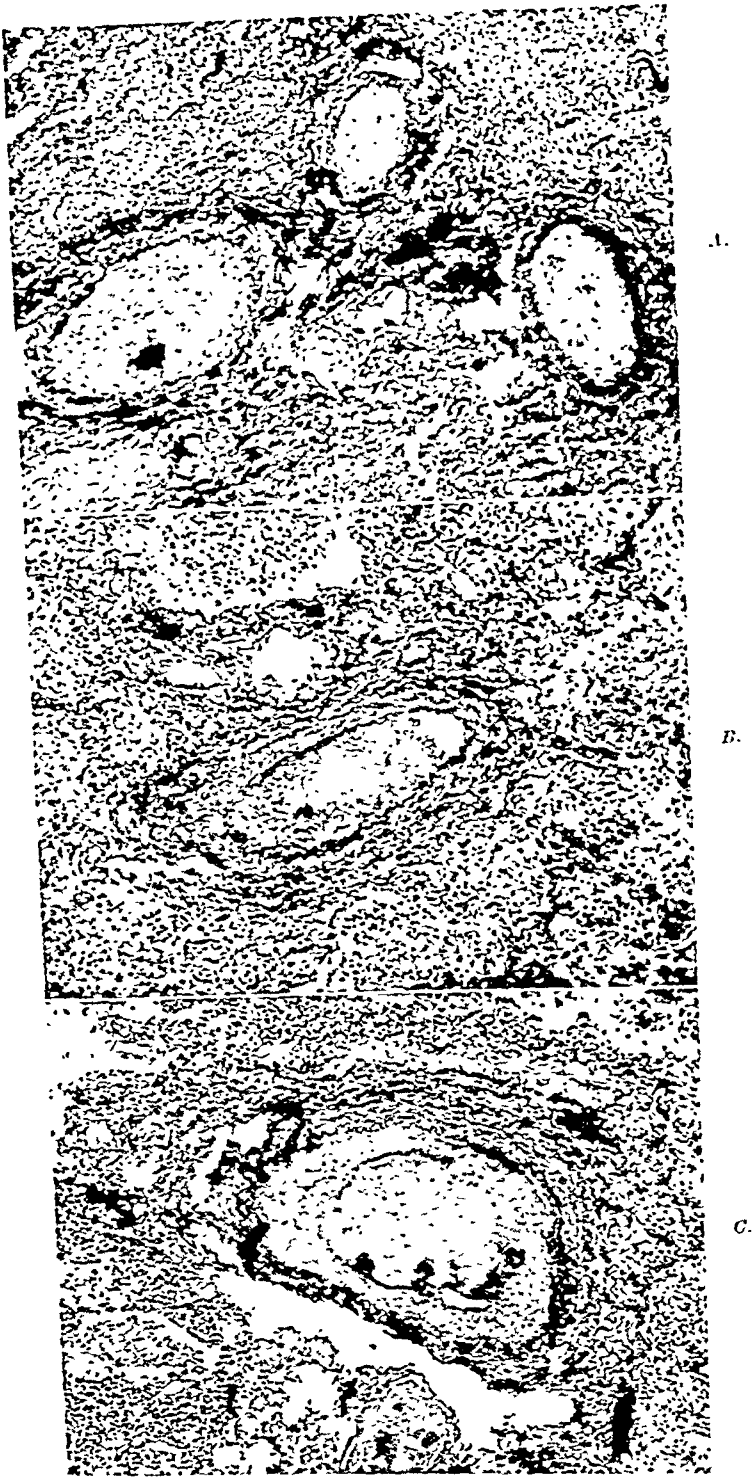
	Normal	Patient
O_2 capacity (vol. %)	19.5-20.5	20.7
O_2 saturation (%)	95-97	*38.1*
CO_2 content (vol. %) (plasma)	54-57	66.8
pH (plasma)	7.38-7.41	7.38
CO_2 tension (mm. Hg)	40.0	50.5

Among the results, the severe arterial hypoxemia stood out, and a massive functional shunt was suspected. The patient died on October 21, the eighth day of illness, vomiting coffee-ground-like material.

The autopsy report (S 1337-57, Professor Werthemann) [italics are ours] stated that there were severe confluent bronchopneumonia and interstitial pneumonia of *both lower lobes and the left upper lobe,* also isolated bronchopneumonic foci of the *right middle and upper lobes,* total obliteration of both pleural cavities with fresh fibrinous pleuritis of the right lower lobe; severe, in part hemorrhagic tracheobronchitis. Fresh mucosal ulcerations of the first duodenal portion were seen also.

The pathologic findings showed that all lung lobes were more or less involved by the pneumonic process.

Sixty-eight microscopic sections taken from the diseased lung portions showed an almost complete obliteration of alveoli and bronchioles by inflammatory exudate, and marked dilatation and congestion of all blood vessels, i.e., capillaries, small and large veins, and arteries (Fig. 1, *A*, *B*, and *C*). Of particular interest were the markedly distended capillaries in the alveolar wall.



All sections were stained with hematoxylin and eosin and Weigert's fuchsin elastic tissue stains.

Fig. 1.—Case 1. *A*, Three markedly distended and congested arteries with numerous capillaries. Alveoli are filled with exudate containing abundant numbers of neutrophils with many histiocytes and erythrocytes. (×70; reduced ⅕.)

B and *C*, Similar histologic picture as in *A*. (×100; reduced ⅕.)

Summary.—A 55-year-old man became ill suddenly and died 8 days later with generalized bronchopneumonia. Blood gas analysis performed 2 days before death showed a markedly reduced oxygen saturation of arterial blood. Detailed microscopic examination of the diseased lung portions showed, in addition to massive pneumonia, severe dilatation and congestion of lung arteries and arterioles.

CASE 2.—A. S., a 22-year-old man, had never been seriously ill. On Nov. 16, 1957, cold and cough, without expectoration, and slight fever developed. In the following days, increase of temperature, tachypnea and chest pain with respiratory movements occurred. On November 18, he was admitted to the hospital in poor general condition, with cyanosis of lips and tongue. Respiration was superficial, with tachypnea, and decreased respiratory sounds on both sides. The temperature was 40° C. X-ray studies of the chest showed bronchopneumonic infiltrates in the right upper lobe and left upper lobe.

Blood gas analysis of arterial blood on November 18 (on the third day of illness and 1 day before death) follows [italics are ours].

	Normal	10 min. without oxygen	20 min. with oxygen
O_2 capacity (vol. %)	19.5-20.5	20.6	20.7
O_2 saturation (%)	95-97	*81.2*	87.5
O_2 tension (mm. Hg)	85-95	43.0	—
CO_2 content (vol. %) (plasma)	54-57	48.5	47.1
pH (plasma)	7.38-7.41	7.49	7.50
CO_2 tension (mm. Hg)	40.0	29.5	28.0

The examination showed, among other findings, a reduced oxygen saturation of arterial blood that increased *only slightly following oxygen breathing.* It was considered likely that a functional vascular shunt and impaired alveolo-capillary diffusion of oxygen had taken place.

The patient was treated with penicillin, streptomycin, hydrocortisone, and analeptic drugs. The blood pressure kept falling and the patient died in cardiovascular collapse on November 19, the fourth day of illness.

The autopsy report (S 1463-57 by Professor Werthemann) [italics are ours] stated that there were severe confluent, hemorrhagic, in part suppurative bronchopneumonia of the *entire left lower lobe, the right upper and lower lobes,* fibrinous pleuritis overlying the pneumonic lung areas, terminal pulmonary edema, severe pseudomembranous hemorrhagic bronchitis and tracheitis.

Virological examination of the involved lung revealed the presence of influenzal virus (*A asiatica*). Bacteriologic examination of the lung showed *Staphylococcus pyogenes* var. *aureus*.

Microscopic examination of the lung (24 sections) displayed a massive obstruction of the alveolar and bronchiolar lumen by pneumonic exudate and a generalized severe congestion and dilatation of all blood vessels, i.e., also of the arterioles and capillaries. The picture was strikingly similar to that seen in the preceding case (Fig. 2, *A, B, C, D, E*).

Summary.—A previously healthy young man became suddenly ill with influenza and died after a course of only 4 days, with bronchopneumonia of

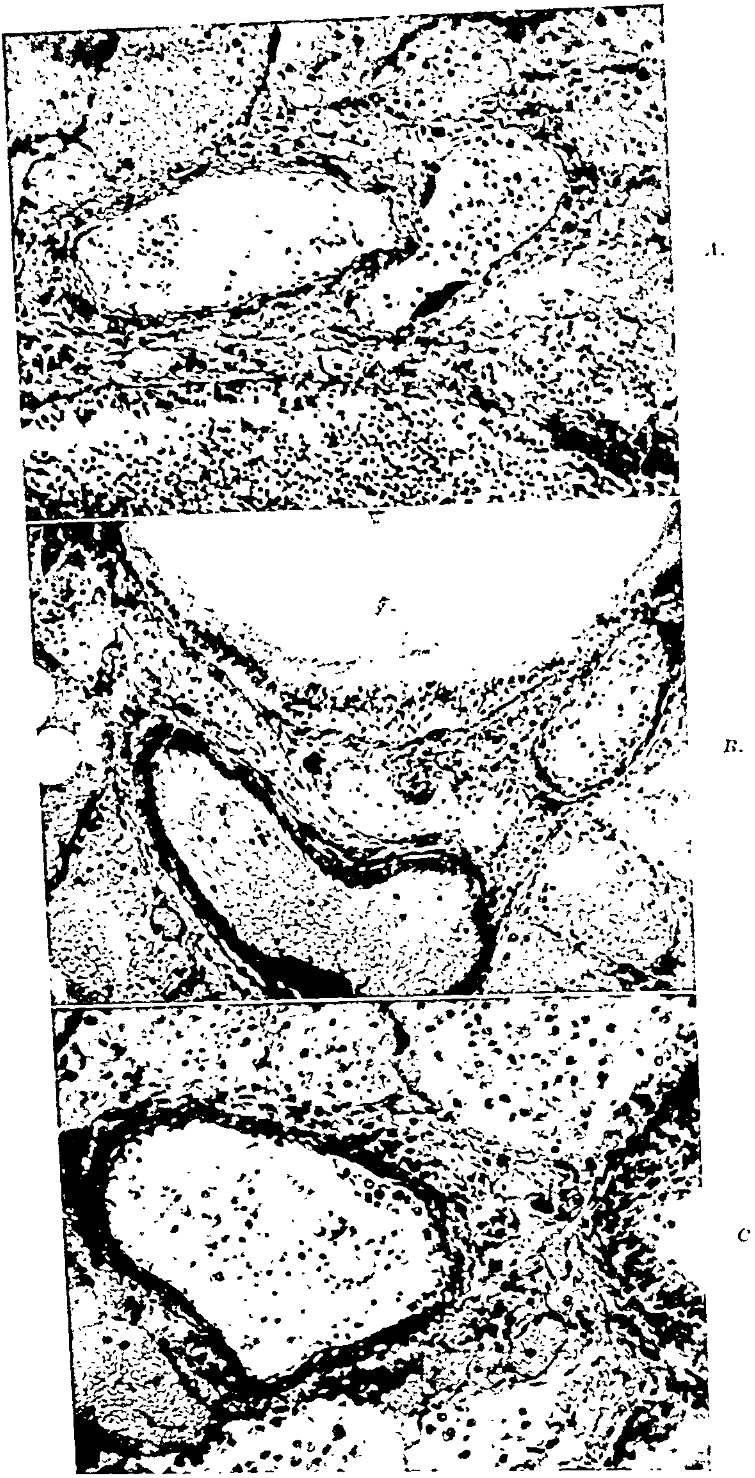


Fig. 2.—Case 2. *A*, *B*, *C*, *D*, and *E*, Marked dilatation of artery and vein. Bronchus contains numerous neutrophils, epithelium is in part desquamated. Alveoli are also distended and filled with blood. Note marked engorgement of interalveolar capillaries. (All magnified ×175, except *C* which is ×270; all reduced ⅕.)

the left lower lobe and the right upper and lower lobes. Blood gas analysis performed 1 day prior to death showed a diminished oxygen saturation of arterial blood which rose but slightly following oxygen breathing and did not reach normal values. Microscopic examination of the diseased pulmonary vessels revealed, besides severe pneumonic infiltrations, a generalized congestion and dilatation of lung arterioles.

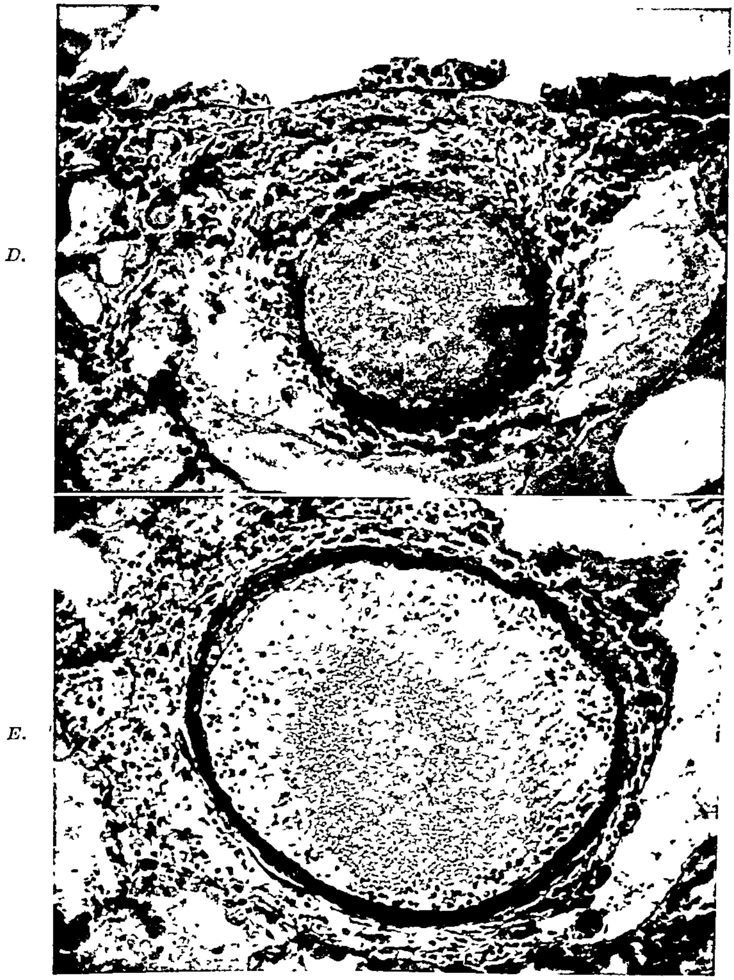


Fig. 2.—Cont'd. *D and E, For legend see preceding page.*

Case 3.—J. M., a 71-year-old man, a former blacksmith, had been hospitalized a year previously for cirrhosis of the liver. He became ill on Nov. 18, 1957, with a fever of 39° C. and cough. On November 21, cyanosis of the lips was observed. Hospital admission occurred on November 22; cyanosis of the tongue was then also noticed. Blood pressure was 220/100 mm. Hg. X-ray studies of the chest showed pneumonic infiltrates of both lower lobes and possibly also of the right middle lobe. The patient was treated with penicillin, strophantin, and analeptic drugs.

On November 23, the sixth day of illness and 1 day prior to death, gas analysis of arterial blood was performed [italics are ours].

	Normal	10 min. without oxygen	20 min. with oxygen
O_2 capacity (vol. %)	19.5-20.5	19.0	19.0
O_2 saturation (%)	95-97	83.0	89.5
O_2 tension (mm. Hg)	85-95	50.4	61.5
CO_2 content (vol. %) (plasma)	54-57	41.0	41.0
pH (plasma)	7.38-7.41	7.38	7.37
CO_2 tension (mm. Hg)	40.0	31.0	31.5

The examination showed among other findings a reduced oxygen saturation of arterial blood that rose slightly following oxygen breathing but did not attain normal values. In spite of oxygen therapy and chloromycetin, the patient become somnolent and died on November 24 with the signs of progressive cardiac insufficiency.

The autopsy report (S 1490-57, Professor Werthemann) [italics are ours] stated that there were severe hemorrhagic, in part fibrinous tracheobronchitis, a lobar, confluent hemorrhagic pneumonia of the *right lower lobe;* confluent nodular hemorrhagic, purulent bronchopneumonia of the *left lower lobe;* moderate edema and severe cyanosis of both lungs. There were also obliteration of the right pleural cavity, hypertrophic cirrhosis of the liver, and hypertrophy of the left ventricle and stenosing coronary sclerosis.

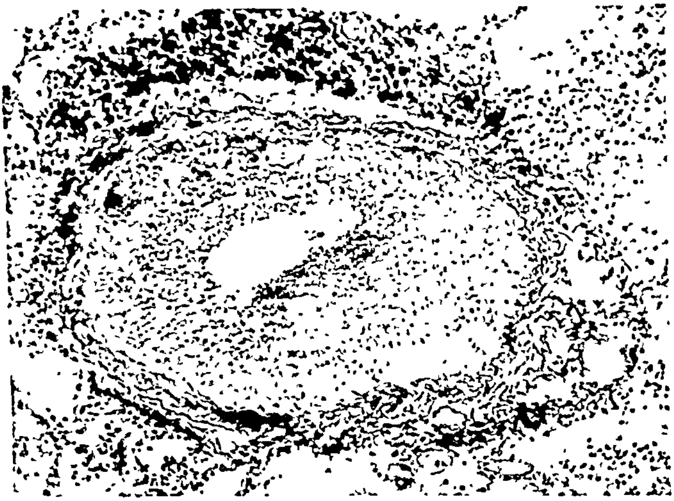


Fig. 3.—Case 3. Marked dilatation and congestion of an artery. Alveoli are filled with exudate consisting of neutrophils and erythrocytes. Deposition of anthracotic pigment. (×110; reduced ⅕.)

Microscopic examination of the diseased lung portions (54 sections) showed —similar to the previous cases—an almost complete obstruction of the alveolar and bronchial lumen by exudate, blood, and edema fluid and a generalized severe dilatation and congestion of all blood vessels, including lung arterioles (Fig. 3).

Summary.—A 71-year-old man with cirrhosis of the liver became ill suddenly with influenza and died 7 days later with lobar pneumonia of the right lower lobe and bronchopneumonia of the left lower lobe. Blood gas analysis performed 1 day before death displayed a reduced oxygen saturation of arterial blood that rose little following oxygen breathing but did not reach the normal value. Microscopic examination of the diseased lung portions showed obliteration of alveolar and bronchiolar lumen by exudate and edema fluid and generalized congestion and dilatation of all blood vessels.

DISCUSSION

The microscopic picture of influenzal pneumonia is characterized in all the cases by a massive infiltration and obstruction of the respiratory passages by exudate with many polymorphonuclear leukocytes, fibrin, many erythrocytes, and edema fluid. The blood vessels are engorged with blood and are markedly distended.

It is a well-known fact that an acute inflammation of vascular organs is followed by dilatation and congestion of local blood vessels as shown clinically by the signs of hyperemia and swelling. The cardinal symptoms of Celsus, i.e., rubor, tumor, calor, and dolor, point to this fact. In an acute inflammatory process in the lung this organ does not act otherwise and hyperemic congestion and dilatation are easy to see. However, these are autopsy findings in a full-blown inflammation and it is not altogether admissible to draw conclusions from these findings regarding vascular reaction in the *early* stages of the illness.

In the present investigation we have been mainly interested in correlating the clinical findings made in the light of blood gas analyses and the pathologic findings after death. The cases just described have several things in common: the stormy course of the illness that takes them all ad exitum within 8 days in spite of their various ages (22, 55, and 71 years, respectively,) and the very similar pathologic findings of influenzal pneumonia. The blood gas analyses were performed in every case 1 or 2 days before death.

When examining the oxygen saturation rates of arterial blood, one is struck by the unusually low value in Case 1–38.1 per cent (normal value 95 to 97 per cent). It is likely that the generalized pneumonia involving all lung lobes was instrumental in reducing the oxygen saturation to such an abnormal level.

In Cases 2 and 3, the oxygen saturation levels were similar, i.e., 81.2 per cent and 83.0 per cent, respectively. This saturation was slightly increased further by breathing pure oxygen. In these 2 cases not all of the lung portions were involved by pneumonic infiltrates as it had been in Case 1, and this may explain in part the different findings in these two groups of cases.

A question that remains unanswered in the present investigation is whether pulmonary arterioles contract in the *early* phases of influenzal pneumonia and thus possibly prevent a functional shunt, an arteriovenous anastomosis.

The experiments of von Euler and Liljestrand[3, 5, 6] who administered air poor in oxygen or rich in carbon dioxide were carried out on animals and human beings whose lungs very likely were not subject to an acute inflammatory process. It is therefore quite possible that lung arterioles in man react to oxygen lack by contracting and that, in such a way, blood is channeled into better aerated lung areas. However, if a massive acute inflammatory process takes place, such as influenzal pneumonia, this mechanism of purposeful blood distribution is probably abolished, the arterioles dilate in order to accommodate the increased blood volume attracted by the inflammatory reaction. A vascular reaction similar to that seen in influenza is equally observed in other types of acute pneumonia. Fig. 4 shows a microphotograph of a case of noninfluenzal bronchopneumonia. Like in influenza, an obvious dilatation and congestion of arteries and veins surrounded by inflammatory exudate in the alveoli and bronchioles is displayed.

Occasionally, blood supply to the diseased lung will be diminished not by arterial contraction but as a result of vascular thrombosis. Now and then we have seen such thrombotic occlusions in influenzal pneumonia especially in the chronic cases. These thromboses are—of course solely from the standpoint of gas exchange in the lung—useful and cause the blood stream to be diverted to noninvolved lung areas.

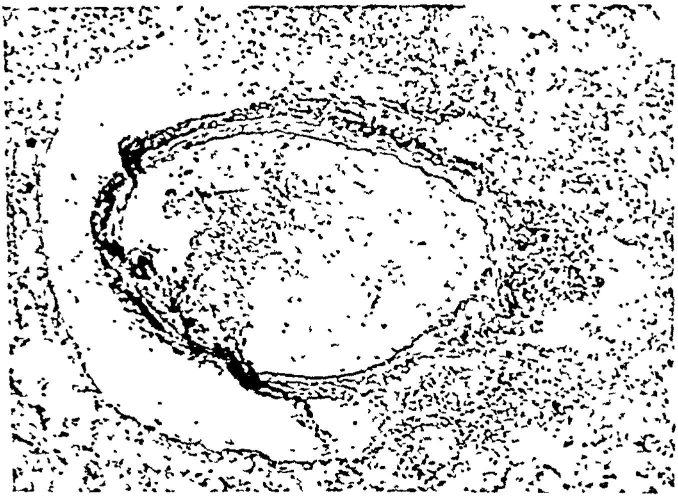


Fig 4.—Nongrippal pneumonia Dilated and congested artery and vein Alveoli filled with exudate. (× 100, reduced ½)

Remarks Regarding Oxygen Therapy of Patients Ill With Influenzal Pneumonia.—If a blood analysis shows that oxygen saturation of arterial blood is lower than normal, and if oxygen breathing does not raise it to normal values or does not affect it at all, it may be assumed that the gas exchange in the lung has been considerably impaired provided, however, that this did not occur as a result of lowered hemoglobin-oxygen binding capacity as for example in anemia (this would be characterized by a diminished oxygen capacity of arterial blood) or of poor respiratory movements, failure of the heart pump or of the respiratory center.

Oxygen respiration is frequently a lifesaving measure in many of the above conditions but fails if for anatomic reasons it is not possible to bring about a gas exchange in the lungs; an example of such a condition can be found in the acute influenzal pneumonia as we have shown it in three examples. Here the extent of inflammation is of course all important. If, as in Case 1, the inflammatory reaction almost completely involves both lungs, it becomes difficult to hope that the oxygen level of arterial blood will rise significantly or even reach normal values as a result of oxygen breathing, since the oxygen is not able to penetrate into alveolar capillaries because of a mechanical blocking of the alveoli.

A more logical therapeutic approach to these conditions, characterized by a low arterial oxygen saturation not responding to oxygen breathing, would consist in oxygenizing blood directly instead of trying to have oxygen cross the blocked alveolo-capillary barrier in order to combine with the hemoglobin of capillary blood.

Already in 1882, von Schröder[7] had tried to oxygenize venous blood flowing through isolated organs. A modern method of oxygenization of venous blood was first suggested by Lillehei, DeWall and co-workers.[8, 9] Its use in operations on the heart and lungs is well established today. Oxygenization of venous blood is carried out in an oxygenator in which oxygen is mixed with venous blood in a special chamber; another important component of this machine is a debubbling device serving to remove the numerous gas bubbles from oxygenized blood to prevent gas embolism.

The main field of application of these oxygenators is naturally in heart surgery where they replace the heart and lung functions during the surgical intervention. In the present cases the problem consists in replacing only the function of the lung in the gas exchange, i.e., in the oxygenization of venous blood.

The technique of an artificial oxygenization of venous blood will have to be tried out, of course, in animal experiments. The duration of oxygen transfusion is limited to a large degree by hemolysis that occurs during such a procedure; moreover, changes in pH and electrolytes of blood occur and have to be corrected. Furthermore, one of the main technical problems of an oxygenator is still a quantitative prevention of gas bubble formation and gas embolism.

If these technical problems could be reduced and eliminated then, in the uncomplicated case, blood could be removed from a vein and run through an oxygenator; the oxygenized blood would then be transfused into another vein from which it would reach the heart and flow through the diseased lungs, circulate in the arteries, and again return to the vein going to the oxygenator. It seems that such a procedure, if the technical problems could be mastered, might not be much more complicated than an ordinary blood transfusion.

The above remarks represents merely a therapeutical suggestion that we are advancing very humbly being aware of the technical problems involved. However, if it were possible to carry out such an artificial oxygenization of venous blood with a simple oxygenator, for a significant length of time without the risk of gas embolism, hemolysis, significant changes in the level of plasma ion concentrations, and the pH of blood, then we would have a new important therapeutical tool with the help of which the 3 patients just reported might have been saved.

Obviously, the method of artificial oxygenization of blood could be applied in many other conditions characterized by a partial or complete loss of lung function, such as generalized lung edema, lungs in drowning, trauma of the thorax, and traumatic lung injuries.

SUMMARY

An attempt is being made to correlate the low oxygen saturation levels of arterial blood in 3 patients dying of influenzal pneumonia with the microscopic findings in their lungs. No vascular contraction—as expected on the basis of experiments done by von Euler and Liljestrand—was seen in the diseased lung areas.

In cases where oxygen breathing is followed by no rise or only a small rise of oxygen saturation levels in the arterial blood, artificial oxygenation of venous blood by means of an oxygenator is suggested as the logical treatment.

I wish to thank Professor Werthemann for allowing me to study autopsy protocols and autopsy material relative to this study, Professor Staub for permission to study and use parts of the case histories, and Dr. Herzog for suggestions regarding blood gas analysis. Microphotographs were made by Mr. Sutter.

REFERENCES

1. Stadie, W. C.: The Oxygen of the Arterial and Venous Blood in Pneumonia and Its Relation to Cyanosis, J. Exper. Med. 30: 215, 1919.
2. Herzog, H.: Die Bedeutung gasanalytischer Untersuchungen im arteriellen Blut und in der Alveolarluft für Diagnose und Therapie bei Grippepneumonie, Praxis 47: 140, 1958.
3. Von Euler, U. S., and Liljestrand, G.: Observations on the Pulmonary Arterial Blood Pressure in the Cat, Acta physiol. scandinav. 12: 301, 1946.
4. Motley, H. L., Cournand, A., Werko, L., Himmelstein, A., and Dresdale, D.: The Influence of Short Periods of Induced Acute Anoxia Upon Pulmonary Artery Pressures in Man, Am. J. Physiol. 150: 315, 1947.
5. Liljestrand, G.: Regulation of Pulmonary Arterial Blood Pressure, Arch. Int. Med. 81: 162, 1948.
6. Von Euler, U. S.: Verhandl. deutsch. Gesellsch. Kreislaufforsch. 17: 8, 1951.
7. Von Schröder, W.: Über die Bildungsstätte des Harnstoffs, Arch. f. exper. Path. u. Pharmakol. 15: 364, 1882.
8. Lillehei, C. V., DeWall, R. A., Read, R. C., Warden, H. E., and Varco, R. L.: Direct Vision Intracardiac Surgery in Man Using a Simple, Disposable Artificial Oxygenator, Dis. Chest 29: 1, 1956.
9. DeWall, R. A., Read, R. C., Warden, H. E., Gott, V., Varco, R. L., and Lillehei, C. W.: A Simple, Disposable, Artificial Oxygenator for Use in Intracardiac Surgery, Surg. Clin. North America 36: 1025, 1956.

BILATERAL INFERIOR DEEP CERVICAL (SCALENE FAT PAD) AND PARATRACHEAL LYMPH NODE BIOPSIES

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Biopsy of the inferior deep cervical lymph nodes, as advocated by Daniels[1] in 1949, has proved to be a worthwhile procedure in the diagnosis of intrathoracic diseases. This operation is usually performed on one side and consists of a partial excision of the scalene fat pad with its associated inferior deep cervical lymph nodes. Steele and Marable[2] have described an excellent method of removing the paratracheal and inferior deep cervical lymph nodes on one side through an incision along the anterior border of the sternocleidomastoideus muscle. We have extended this procedure and at present it is our policy to perform bilateral inferior deep cervical and paratracheal lymph node biopsies through a single incision.

TECHNIQUE

The patient is placed in the supine position and the neck is extended by placing a folded sheet beneath the shoulders. With the surgeon on the left side, a transverse incision is made about 3 cm. above the suprasternal notch (Fig. 1, *1*). The ends of this incision should be located slightly lateral to the anterior border of each sternocleidomastoideus muscle. The incision is extended through the platysma muscle and the upper and lower flaps are undermined in the subplatysmal plane. The investing layer of the deep cervical fascia is incised vertically in the midline avoiding the anterior jugular veins and the jugular venous arch (Fig. 1, *2*). The sternohyoid and sternothyroid muscles are retracted laterally to expose the pretracheal layer of the deep cervical fascia. This fascia is incised vertically in the midline avoiding the underlying inferior thyroid veins and exposing the trachea in the superior mediastinum (Fig. 1, *3*). Lymph nodes with their accompanying adipose tissue from the right and left paratracheal areas are dissected free and removed.

The right scalene fat pad with its associated inferior deep cervical lymph nodes is partly excised by removing its medial and inferior portions which are adjacent to the internal jugular and subclavian veins. This is accomplished by retracting the sternocleidomastoideus muscle anteriorly and laterally after the

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investing layer of the deep cervical fascia along its anterior border has been incised for a short distance. The sternohyoid and sternothyroid muscles are retracted medially. The pretracheal fascia, forming the anterior portion of the carotid sheath, is incised longitudinally exposing the internal jugular vein which is retracted medially (Fig. 1, *4*). The scalene fat pad is palpated anterior to the scalenus anticus muscle in the subclavian triangle. The scalene fat pad is dissected off the prevertebral fascia covering the scalenus anticus muscle thus exposing the phrenic nerve (Fig. 1, *5*). It is also dissected off the proximal portions of the internal jugular and subclavian veins. The inferiomedial portion of the scalene fat pad with its associated inferior deep cervical lymph nodes is then excised.

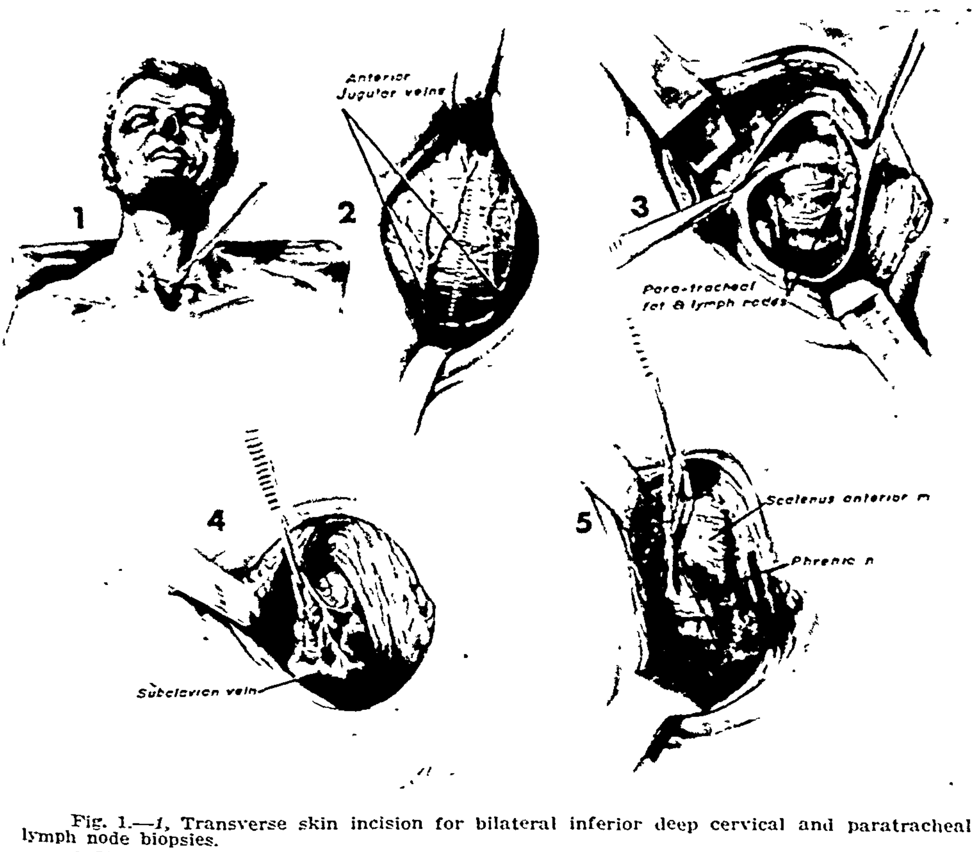

Fig. 1.—*1*, Transverse skin incision for bilateral inferior deep cervical and paratracheal lymph node biopsies.

2, Vertical midline incision through the investing layer of the deep cervical fascia.

3, Vertical midline incision through the pretracheal fascia exposing the trachea.

4, Exposure of the right scalene fat pad obtained by retracting the sternocleidomastoideus muscle anteriorly and laterally, and the internal jugular vein medially.

5, Exposure of the right scalenus anticus muscle with its overlying phrenic nerve after the scalene fat pad has been removed.

The surgeon now moves to the right side of the table and the left scalene fat pad is removed in a similar manner. Particular care is exercised to prevent injury to the thoracic duct. Lymph nodes from the four different areas of biopsy are placed in separate specimen jars. After complete hemostasis is obtained in all four areas of biopsy, the investing layer of the deep cervical fascia is approximated in the midline by interrupted sutures. The skin flaps, including the platysma muscle, are approximated with one layer of interrupted sutures placed so that the knots are buried in the subplatysmal plane. The superficial portion of these sutures is located in a subcuticular position and no skin sutures are used. A pressure dressing completes the procedure.

SUMMARY

A method of biopsy in which both the right and left inferior deep cervical and paratracheal lymph nodes are removed through a single incision is described. This eliminates a second biopsy through a separate incision on the opposite side. We believe that a greater number of positive diagnoses will be made when both right and left inferior deep cervical and paratracheal lymph nodes are biopsied routinely.

REFERENCES

1. Daniels, A. C.: Method of Biopsy Useful in Diagnosing Certain Intrathoracic Diseases, Dis. Chest 16: 360-366, 1949.
2. Steele, J. D., and Marable, S. A.: Cervical Mediastinotomy for Biopsy, J. THORACIC SURG 37: 621-624, 1959.

SURGICAL RESECTION IN PULMONARY TUBERCULOSIS DUE TO ATYPICAL MYCOBACTERIUM TUBERCULOSIS

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EXPERIENCE with over 180 cases of atypical pulmonary tuberculosis, treated with conventional antituberculosis drug therapy at Battey State Hospital, has shown the conversion rate to be about 22 per cent. In typical tuberculosis, the conversion rate is about 90 per cent after 6 months of drug therapy. In atypical tuberculosis, the great shortcomings of this medical approach have led us to continue excisional surgery in selected cases. Our experience would indicate that resection can be done with a low morbidity and a reasonably low mortality with resultant high sputum conversion in well-chosen cases and affords reasonably good results in the long-term tenure.

MATERIALS AND METHODS

From Jan. 1, 1950, to the end of April, 1959, 25 patients with atypical tuberculosis were subjected to pulmonary resection. Of the 23 white patients, 18 were male and 5 were female. The 2 Negro patients were male. Twelve patients subjected to resection were in their forties; 6 were in their thirties; 5 were in their fifties; and the youngest patient was 28 and the oldest 67 years of age.

According to the classification of the National Tuberculosis Association, the disease was minimal in 1 case, moderately advanced in 13, and far advanced in the remaining 10 cases.

On admission bacteriologic studies, 16 of the patients were positive by both direct smear and culture and 9 were negative on direct smear but positive on culture. Using Runyon's classification,[1] 22 of the positive cultures were nonphotochromogenics (Group III-Battey type). In 2 patients, there were photochromogenic strains (Group I), and in 1 there was a scotochromogenic strain (Group II).

As soon as a working diagnosis of pulmonary tuberculosis was established, 24 of the 25 patients were placed on antituberculous drug therapy. Twelve of these patients received isonicotinic acid hydrazide (INH) and para-aminosalicylic acid (PAS), 9 received INH, streptomycin, and PAS, 3 received streptomycin and PAS, and 1 patient received INH, streptomycin, PAS, and Dalicin

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in the preoperative period. Additional chemotherapy was used in the postoperative period. Ten of the 12 patients having had INH and PAS received streptomycin in the postoperative period. Another patient who received INH and PAS had pyrazinamide (PZA) added in the postsurgical period. There was 1 patient who received no drug therapy before or after surgery.

Two patients had no sensitivity studies done prior to surgery. Of the 23 patients who did have, 23 were completely resistant to isoniazid, and 13 of these 23 were totally resistant to streptomycin–5 were partially sensitive, and 5 were completely sensitive to streptomycin on the last studies done prior to surgery.

Four of the 25 patients had negative sputum studies at the time of surgery; 1 patient had been negative for 3 months, 2 for 5 months, and 1 for 10 months. Of the remaining 21 patients, 2 were intermittently positive and 19 had never had negative cultures.

Twenty-three of these patients had preoperative bronchoscopies. One had a partial stenosis of the right upper lobe bronchus. One patient had severe endobronchitis which required postponement of surgery for 2 months until the inflammatory process had subsided under treatment. Resection was then successfully performed. Five of these patients had bronchograms. One revealed extensive bronchiectasis of the left lung and this patient eventually had a left pneumonectomy.

Twenty of the 25 patients were operated upon for open cavities plus positive sputum. One patient had an open cavity and a negative sputum, 1 patient had residual fibrocaseous disease and a positive sputum, 3 patients had residual fibrocaseous disease with a negative sputum.

There were 26 resections performed on these 25 patients (Table I). One patient had a right upper lobectomy first followed 20 days later by a segmentectomy by the removal of the upper division of the left upper lobe.

TABLE I. SURGICAL PROCEDURES

PROCEDURES	NO.	WITHOUT COMPLICATION	WITH COMPLICATION	DEATH
Subsegmentectomy	4	3	1	0
Segmentectomy	7	6	1	0
Lobectomy, alone	10	9	1*	1
Lobectomy, plus	3	1	2*	2
Pneumonectomy	2	2	0	0
Total	26	21	5	3

*In these cases, the complications were followed by death.

MORBIDITY AND MORTALITY

The patient who had bilateral resections had an uncomplicated course following each resection. Five patients (20 per cent) had postoperative complications (Table II). One of the 4 subsegmental resections was followed by a bronchopleural fistula which required post-resection thoracoplasty. One of the 7 segmental resections was also complicated by a bronchopleural fistula and residual space problem that required a post-resection thoracoplasty. There were no deaths in the 11 patients who had small resections.

TABLE II. MORBIDITY AND MORTALITY DUE TO SURGICAL COMPLICATION

PROCEDURES	COMPLICATION	MORTALITY	POSTOP. SPUTUM STATUS
1. Subsegmentectomy, apical posterior segment, LUL, with post-resection thoracoplasty	Bronchopleural fistula and residual space		Sputum converted 28 months after surgery
2. Segmentectomy, apical posterior segment, RUL, with post-resection thoracoplasty	Bronchopleural fistula and residual space		Sputum converted following surgery
3. RUL lobectomy plus segmentectomy, superior segment, RLL	Pneumonia	Died of pneumonia on seventh postop. day	
4. RUL and RML lobectomies plus wedge of superior segment, RLL, with post-resection thoracoplasty	Bronchopleural fistula and residual space	Died of pulmonary insufficiency on fourth postop. day	
5. RUL lobectomy	Pulmonary insufficiency	Died of hypoxia, 48 hours	
Total		5 Cases	

Of the 10 patients who had lobectomy only, 9 had no complications. One patient died of pulmonary insufficiency 48 hours after a right upper lobectomy. There were 3 patients who had lobectomies plus removal of other lung tissue, and 2 of these procedures were accompanied by complications which led to death. One was a 67-year-old white woman who had a right upper and a right middle lobectomy plus removal of a wedge from the lower lobe. There was not enough tissue to adequately fill the pleural space and a post-resection thoracoplasty was performed 3 weeks after the resection. Following this, the patient died of pulmonary insufficiency on the fifth postoperative day. Another patient, having had a right upper lobectomy plus a superior segmental resection of the superior division of the right lower lobe, died on the seventh postoperative day of pneumonia and atelectasis on the operative side, which was revealed at autopsy. There were 2 patients who had pneumonectomies and both had uncomplicated courses postoperatively. The surgical mortality rate, therefore, was 12 per cent.

Pathologic and bacteriologic studies of the surgical specimens revealed 2 surgical specimens negative on direct smear and culture. Twenty-four of the 26 surgical specimens had positive direct smears and, of these, 18 were positive on culture. According to C. Edwin Smith, Battey Laboratory Director, these cultures were the same in each case as had been isolated preoperatively from each individual. Dr. I. Stergus, Pathologist at Battey State Hospital, says that "Pathologically, these lesions are indistinguishable from those of typical tuberculosis, grossly and microscopically."

RESULTS

Four of the 25 patients had negative sputum at the time of surgery which remained consistently negative following surgery. Of these 4 patients who had negative sputum, 1 had an open cavity and the other 3 had residual fibrocaseous disease. Whether or not the sputum of these 4 patients would have remained negative without surgery cannot be stated, but we count these 4 patients as combined medical-surgical treatment successes.

The sputum was positive in 21 patients at the time of surgery. In 14 cases, it converted immediately following surgery and has remained negative. We consider these 14 successes primarily attributable to surgery. There were 3 more patients who had cavitary disease with positive sputum at the time of surgery which did not convert immediately following surgery. The sputum of 1 patient converted within 3 months with new chemotherapy and in the other 2 converted after longer periods of chemotherapy. These successes are also attributed to combined surgical-medical therapy. Our failures are limited to 3 patients who died as a result of their surgery. We believe that 22 of the 25 patients, or 88 per cent, who are now alive and with negative sputum, are treatment successes with the main credit being given to the addition of surgical therapy (Table III).

TABLE III. SPUTUM STATUS FOLLOWING SURGERY

	NO.	PER CENT
Negative before and after surgery	4	16
Positive prior to surgery and negative thereafter	14	66
Positive prior to surgery and after surgery but still converted subsequently	4	16
Positive prior to surgery and died as a result of surgery	3	12
Total	25	100

DISCUSSION

In judging surgical therapy, one has to weigh the risk of surgery against the risk the patient must take without this treatment. In the group of patients at Battey State Hospital with atypical tuberculosis, only 20 per cent have been treated successfully by chemotherapy alone. In this small group of 25 patients treated by surgery and chemotherapy, 88 per cent have been treated successfully. It is our belief that patients who are surgical candidates should be subjected to resection as soon as possible. We have not attempted to reach a target point of negativity in this group.

The surgical mortality rate was 12 per cent. Up to the present time, there have been 31 deaths in the 155 patients treated medically, for a mortality rate of 20 per cent. In this medically treated group, 8 patients have died of atypical pulmonary tuberculosis, 7 have died of cardiac disease, and 13 have died of pulmonary tuberculosis and cardiac failure.

In a previous publication,[2] we suggested that resections of less than a lobe were unsatisfactory. With a somewhat larger experience, we found a complication rate of 20 per cent in resections of less than a lobe, and there were no deaths in this group. Although bronchopleural fistulas are serious complications, they are amenable to post-resection thoracoplastics. We believe that smaller resections may be used wherever indicated.

The deaths in our group of patients followed lobectomy plus segmental resection and/or wedge resections. Two of these three deaths might have been averted. The patient who had had a right upper and right middle lobectomy plus a wedge resection of the superior segment of the right lower lobe could have been treated better by a pre-resection thoracoplasty and then completion of the thoracoplasty and tailoring of her chest to fit the remaining lung tissue at the time of the resection. The patient who died from pulmonary insufficiency following a right upper lobectomy might not have been subjected to surgery if a more detailed preoperative pulmonary function evaluation had been made.

SUMMARY

1. Twenty-two of 25 cases of atypical tuberculosis are alive and well following combined surgical-medical therapy.
2. The morbidity rate was 20 per cent. Three patients had bronchopleural fistulas, 2 of whom were successfully treated by post-resection thoracoplasty.
3. There were 3 postoperative deaths.
4. Early resection is advocated in suitable candidates.
5. Resections of less than a lobe are also advocated when indicated.

REFERENCES

1. Runyon, E. H.: Anonymous Mycobacteria in Pulmonary Disease, M. Clin. North America 43: 273-290, 1959.
2. Crow, H. E., King, C. T., Smith, C. E., Corpe, R. F., and Stergus, I.: A Limited Clinical, Pathologic, and Epidemiologic Study of Patients With Pulmonary Lesions Associated With Atypical Acid-Fast Bacilli in the Sputum, Am. Rev. Tuberc. 75: 199-222, 1957.

THE DEVELOPMENT OF BRONCHOGENIC CARCINOMA IN PATIENTS WITH PULMONARY TUBERCULOSIS

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Memphis, Tenn.

THERE has been considerable discussion in the past concerning the simultaneous occurrence of pulmonary tuberculosis and bronchogenic carcinoma.[1-4] Recent interest in this problem reflects the presumption that the incidence of bronchogenic carcinoma may be higher in patients with pulmonary tuberculosis than in the general population. This led us to review and analyze the 11,000 cases of pulmonary tuberculosis and 650 cases of bronchogenic carcinoma seen at Kennedy Hospital between the years 1947 and 1958.

During this 10-year period, 24 patients with proved pulmonary tuberculosis and bronchogenic carcinoma were seen. Active pulmonary tuberculosis unquestionably existed prior to the onset of the carcinoma in 10 patients, while active pulmonary tuberculosis was present when the carcinoma was discovered in 14 patients. Activity is considered real when two or more positive cultures for acid-fast bacilli are established.

Three additional patients with bronchogenic carcinoma were eliminated from this series. There was 1 patient with a single positive culture and 16 negative cultures. The second patient had three positive smears, but no positive cultures. The third patient was dropped, even though areas of active tuberculosis were found at postmortem, because smears and cultures of his sputa were not obtained.

Age.—Ages of these 24 patients ranged from 31 years to 68 years with a mean age of 58 years. Those with active tuberculosis had a mean age of 54 years, as compared to a mean age of 62 for those classified as having inactive disease.

Sex and Race.—Of the 24 patients, 22 were white males and 2 were Negro males. These figures do not represent actual age and race incidence, because the hospital population is overwhelmingly male.

Site of the Bronchogenic Carcinoma.—Bronchogenic carcinoma and tuberculosis occurred in the same lung in 19 patients. In 16 cases (66 per cent), the two diseases occurred in the same lobe. The carcinoma developed in a site other

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than that involved by tuberculosis in 8 patients. In 5 of these patients the disease had been considered inactive from 2 to 16 years, and active in 3 patients.

Duration of Tuberculosis.—Six patients with active pulmonary tuberculosis were found to have coexisting bronchogenic carcinoma within 6 months after the establishment of the diagnosis of tuberculosis. Another 6 patients were found to have carcinoma 1 to 10 years after the diagnosis of active tuberculosis was established. Two patients had had active disease for more than 10 years at the time that the carcinoma was discovered. All of the patients with inactive tuberculosis had been considered inactive for 2 to 10 years when the bronchogenic carcinoma was found.

Diagnostic Aids.—Bronchoscopy and cytology were utilized in 16 patients. Bronchoscopically, a positive biopsy was obtained in 4 patients (25 per cent), visual evidence of tumor without biopsy was seen in 5 patients (31 per cent), and a negative examination was present in 7 patients (44 per cent). Suspicious cytology was present in 2 patients (12 per cent), positive cytology in 5 patients (31 per cent), and negative cytology in 9 patients (56 per cent).

Diagnosis.—The diagnosis of bronchogenic carcinoma presents many difficulties in patients with pulmonary tuberculosis.[5] The infection usually dominates the clinical picture so that neoplasm is frequently overlooked for varying periods of time. When active tuberculosis was present, the earliest diagnosis of coexistent bronchogenic carcinoma was made in 4 patients after 3 months of hospitalization and antituberculosis chemotherapy; in 1 patient after 6 months; in 7 patients after 1 or more years of hospitalization and treatment. The diagnosis was more rapidly made in the group with inactive disease.

A diagnosis of carcinoma was never made during life in 3 patients. These 3 patients were hospitalized 4 months, 8 months, and 12 months, respectively. All patients had x-ray studies at regular intervals (at least once a month). Two patients had active tuberculosis and in a third patient the disease was considered to be inactive.

Treatment.—Seven patients were subjected to exploratory thoracotomy. In 6 of these, the neoplasms were resected, three by pneumonectomy and three by lobectomy. Two of the pneumonectomy patients and one of the lobectomy patients received ancillary treatment in the form of radiation therapy or nitrogen mustard, and 1 patient received both nitrogen mustard and radiation therapy.

Results.—All patients except 1 are now dead. The survivor had a right upper lobectomy for alveolar cell carcinoma on Sept. 24, 1956. Only 2 other patients lived longer than 10 months after the diagnosis of carcinoma was established. Both of these patients died 15 months after treatment.

DISCUSSION

From postmortem examinations of tuberculosis patients, Gerstl and his associates[6] found bronchogenic carcinoma in 0.44 per cent, while Robbins and

Silverman[7] reported an incidence of 1.5 per cent. Bronchogenic carcinoma has been found in 0.38 per cent of the patients with active tuberculosis seen during the past 8 years at the Mississippi State Sanatorium.[8] The series reported here represents an incidence of 0.2 per cent. This is 20 times greater than the incidence reported in the general population and is comparable to that reported for heavy smokers as described by Pack and Ariel.[9] The autopsy incidence reported in 1946 by Gerstl[6] was 0.44 per cent, while the incidence reported for the general population was only 0.0058 per cent. These figures denote a higher bronchogenic carcinoma rate in patients with pulmonary tuberculosis. Inasmuch as tuberculosis presently tends to appear more frequently in the older patients (over the age 45), these two diseases can be expected to occur together more frequently in the future.[10, 11]

Since the therapeutic results in this series were extremely poor, a search of the clinical records and x-ray films was made to ascertain if there were any clinical or radiologic evidences which would have permitted earlier recognition of the malignancy.

Some of the following clinical and radiologic findings should make one suspicious of a possible coexistent neoplasm in tuberculosis patients: (1) if, after a reasonable trial of antituberculosis chemotherapy, there is no improvement of the patient's general and radiologic status, (2) enlargement of the hilar area, especially if unilateral,[12, 13] (3) atelectasis of a lobe or segment of the lung,[13, 14] (4) solitary nodular density, especially if it is in the lower lobes and has a fuzzy border, and (5) cavities with a thick, irregular wall and a poorly visualized, eccentrically placed, radiolucent central area.

SUMMARY

1. A study of case histories of 11,000 patients with tuberculosis and 650 patients with bronchogenic carcinoma was made in an attempt to establish the relative incidence of the coexistence of these two disease processes in the same patient.

2. The findings indicate that this combination of diseases occurs 20 times more frequently in the patient with tuberculosis than in the patient from the general population.

3. The study suggests that this incidence may increase as the age of the tuberculous patient becomes older.

4. All male patients with tuberculosis over the age of 45 should be studied frequently by clinical and radiologic examinations in the quest for location of the malignant lesion, in addition to the infection. Any suspicion should then invoke a complete investigation to prove the existence or nonexistence of the two lesions.

REFERENCES

1. Carey, J. M., and Greer, A. E.: Bronchogenic Carcinoma Complicating Pulmonary Tuberculosis: A Report of Eight Cases and a Review of 140 Cases Since 1932, Ann. Int. Med. 49: 161-180, 1958.

2. Hamilton, C. E., and Wexler, N. H.: Carcinoma and Tuberculosis of the Lung, Am. Rev. Tuberc. 42: 334-342, 1940.
3. Nuessle, W. F.: Association of Bronchogenic Carcinoma and Active Pulmonary Tuberculosis, Dis. Chest 23: 207-216, 1953.
4. Meyer, E. C., Scatliff, J. H., and Lindskog, G. E.: The Relation of Antecedent Tuberculosis to Bronchogenic Carcinoma: A Study of the Tuberculin Test, Radiologic and Pathologic Evidences, J. Thoracic Surg. 38: 384-397, 1959.
5. Goldberg, J., Figueras, E. R., and Barshay, B.: Coexistent Bronchogenic Carcinoma and Active Pulmonary Tuberculosis, Dis. Chest 21: 184-193, 1952.
6. Gerstl, B., Warring, F. C., Jr., and Howlett, K. S., Jr.: Cancer and Pulmonary Tuberculosis. Diagnostic Problems in Patients With Cancer of the Lung in the Presence of Pulmonary Tuberculosis, Am. Rev. Tuberc. 54: 470-487, 1946.
7. Robbins, E., and Silverman, G.: Coexistent Bronchogenic Carcinoma and Active Pulmonary Tuberculosis, Cancer 2: 65-97, 1949.
8. Wofford, J. L., Stauss, H. W., and Webb, W. R.: Primary Lung Cancer Complicating Tuberculosis. Paper given at the meeting of the Southern Thoracic Surgical Association, Nov. 28, 1958, Miami Beach, Florida.
9. Pack, G. T., and Ariel, I. M.: A Half Century of Effort to Control Cancer. An Appraisal of the Problem and an Estimation of Accomplishments, Internat. Abstr. Surg. 100: 309-352; 425-457; 526-552, 1955; in Surg. Gynec. & Obst., April, May, June, 1955.
10. Sakula, A.: Carcinoma of Bronchus in Association With Active Pulmonary Tuberculosis, Brit. M. J. 1: 759-762, 1955.
11. Shefts, L. M., and Hentel, W.: Bronchogenic Carcinoma and Pulmonary Tuberculosis, Am. Rev. Tuberc. 61: 369-386, 1950.
12. Shafran, M. E., and Kavee, J.: The Diagnosis of Bronchogenic Carcinoma in Patients With Pulmonary Tuberculosis, Arch. Int. Med. 96: 157-167, 1955.
13. Hauser, H., and Glazer, N. M.: Coexistent Tuberculosis and Carcinoma of the Lung, Radiology 65: 680-690, 1955.
14. Cohen, A. C.: Tuberculosis and Carcinoma of the Lung, Dis. Chest 15: 607-611, 1949.

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BILATERAL SIMULTANEOUS SQUAMOUS CELL CARCINOMA OF THE LUNG

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CARCINOMA of the lung is one of the most common tumors of the adult male. The occurrence of bilateral simultaneous primary squamous cell carcinoma arising from major bronchi in a living patient is unknown.[1] Individual cases have been reported in which pulmonary resection was carried out for carcinoma of the lung and years later a malignancy was found in the other lung.[2] Cases have been reported in which carcinoma in situ, a suspected precursor of cancer of the lung, has been found in areas of the same or the opposite lung after pulmonary resection for frankly invasive carcinoma.[3, 4] The presence of squamous cell carcinoma in one lung and a small cell or oat cell carcinoma in the opposite lung has been reported.[1] In all of these cases the diagnosis of bilateral pulmonary malignancy was made partially, if not completely, on the basis of pathologic examination of the resected specimen and examination of autopsy material. A diagnosis of bilateral simultaneous primary squamous cell carcinoma of the lung in a living patient has not been reported in the literature.

CASE REPORT

A 60-year-old white male laborer (I. C. H.) developed a cough productive of yellow-white sputum 3 years prior to admission to the hospital. Fifteen months before hospitalization he developed a cold, pleuritic pain, fever, chills, night sweats and had an increase in cough and sputum. These symptoms subsided in 2 weeks but anorexia persisted. Six months before hospitalization the patient first noted the onset of exertional dyspnea and the recurrence of cough with yellow-white sputum. Three months later he developed intermittent fever, increasing anorexia, constipation, weakness, and had a 10-pound weight loss. These symptoms progressed and 1 month before admission x-ray studies of the chest demonstrated bilateral apical "exudative" pulmonary disease. Sputum examinations were negative for acid-fast bacilli but the roentgenogram was so suggestive of pulmonary tuberculosis that he was admitted to the Ohio Tuberculosis Hospital for diagnosis and treatment.

A roentgenogram of the chest made 7 years prior to admission was reported as normal. The patient smoked one package of cigarettes per day, was treated for syphilis in 1952, and had a 40-year history of alcoholism requiring hospitalization on three occasions. He denied alcoholic intake for the previous 3 years.

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The patient was a well-developed white man with normal vital signs, who appeared chronically ill. There were normal breath sounds over both lung fields and no râles were heard. The liver was firm, nodular, nontender, and enlarged 2 fingerbreadths below the right costal margin. The prostate was enlarged, soft, and nontender on rectal examination. The remainder of the physical examination was within normal limits.

Admission hemoglobin was 11.2 Gm. per cent, hematocrit 39 per cent, white blood cell count 6,850 cells per cubic millimeter with a normal differential. Urinalysis and blood chemistries were normal. Histoplasmosis skin test was positive 20 by 20 mm. PPD No. 1, intermediate, PPD No. 2 and old tuberculin skin tests for tuberculosis were negative. Serologic test was positive for syphilis. Sputum smears and cultures for tuberculosis were negative.

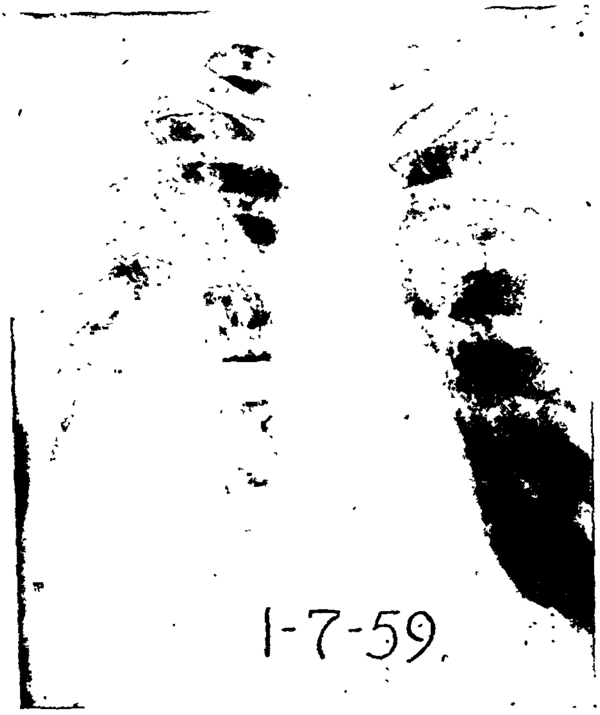
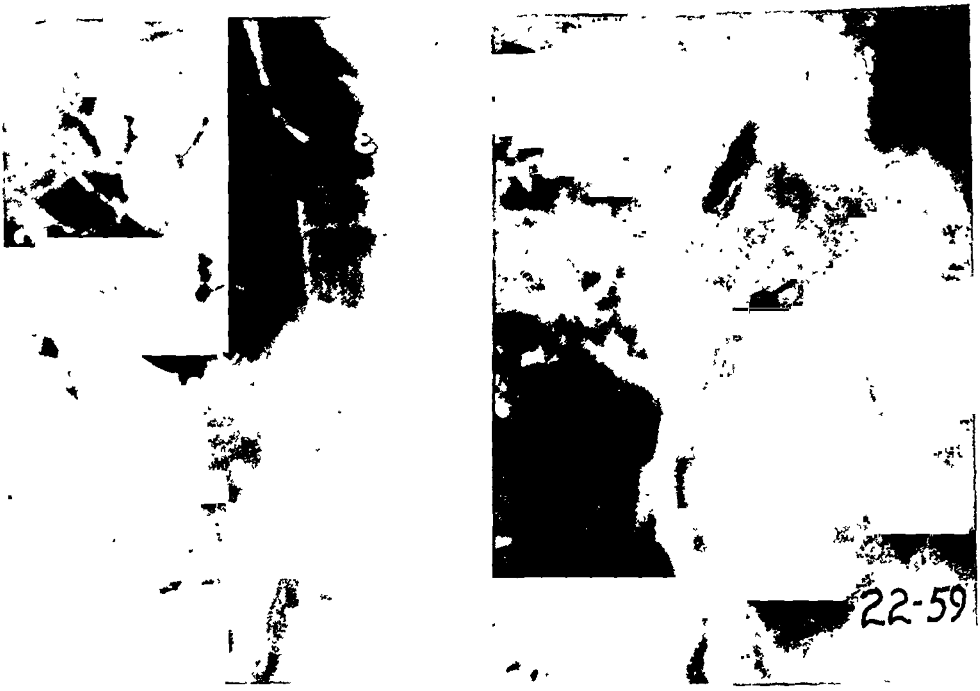


Fig. 1.—*Note the bilateral hilar lymph node enlargement, the soft tissue mass above the right hilum, and linear atelectatic changes in both infraclavicular areas.*

The pre-admission chest roentgenogram on Nov. 20, 1958, demonstrated a soft tissue mass in the right infraclavicular area adjacent to the hilum. Linear and nodular infiltrations were present in both upper lobes. Both hila showed lymph node enlargement. Additional findings were aortic arch calcification, healed fractures of the left sixth and seventh ribs, and left pleurodiaphragmatic adhesions. A roentgenogram of the chest on Jan. 7, 1959, showed the previously described infiltrations in the infraclavicular regions of both upper lung fields (Fig. 1). The soft tissue mass adjacent to the right hilar area was again noted, with bilateral lymph node enlargement, but with no evidence of cavitation.

A bronchoscopy on Jan. 14, 1959, showed the left lower lobe bronchus and its segmental bronchi to be normal. The left upper lobe bronchus appeared normal for 1 cm. when visualized through a right angle telescope. The right lower lobe and middle lobe bronchi were also normal. Thick green purulent secretions were seen obstructing the anterior segmental bronchus of the right upper lobe bronchus. Aspiration of this material did not result in complete clearing of the area of obstruction. A biopsy from the right upper lobe carina was reported to be normal bronchial tissue with squamous metaplasia. Biopsy of the left upper lobe carina showed slight chronic nonspecific bronchitis. Culture of the aspirate was negative for acid-fast bacilli but a moderate growth of hemolytic *Staphylococcus albus* and streptococci was obtained.

A bilateral bronchogram on Jan. 22, 1959, demonstrated obstruction of the posterior and anterior segments of the right upper lobe with partial atelectasis corresponding to the obstructed segments (Fig. 2, *A*). The apical segment of the right upper lobe and the segmental bronchi of the right middle and lower lobes were well outlined. On the left side there was complete obstruction of the left upper lobe bronchus, including the lingula (Fig. 2, *B*). All bronchi of the left lower lobe were well visualized. Other changes in both lung fields were compatible with chronic bronchitis and emphysema. A repeat bronchogram was performed following bronchoscopic aspiration of mucus plugs and aerosol therapy to rule out the possibility of tumor. The same areas of bronchial obstruction were demonstrated which indicated probable bilateral bronchogenic tumors.



A. *B.*

Fig. 2.—*A*, Bronchogram of the right side shows obstruction of the posterior and anterior segments of the right upper lobe. Only the apical segment is patent. *B*, Note the complete obstruction of the left upper lobe bronchus (*arrow*).

On Feb. 2, 1959, a second bronchoscopy was performed to obtain bronchial secretions for cytologic examination. The right upper lobe segmental bronchi were successfully aspirated and an intrabronchial lesion could not be demonstrated. The left main bronchus was narrowed and edematous. The left upper lobe bronchus was visualized and the anterior segmental bronchus aspirated, revisualized, and an obstruction was not seen. Generous biopsies were obtained from the right upper lobe carina and the left upper lobe carina. The bronchial secretions were collected separately during the procedure from the right main bronchus, then from the left main bronchus, and examined for the presence of malignant cells.

Microscopic examination of the biopsy specimen from the right upper lobe carina demonstrated squamous cell carcinoma in the bronchial submucosa. T[illegible] [illegible]sy fro left upper lobe bronchus was unsatisfactory and consisted of cartilage. The bronchial aspirate demonstrated anaplastic tumor cells in the bronchial secretions from both sides.

On Feb. 11, 1959, bronchoscopy was carried out again to obtain a biopsy from the left upper lobe carina. There was no evidence of tumor visualized on the right side and no significant changes were noted. The segmental bronchi of the left upper lobe bronchus were again partially occluded with green exudate in the anterior segmental bronchus. This was aspirated and an obstruction was not visualized. A generous biopsy of the left upper lobe carina was obtained from multiple sites and submitted for microscopic examination. This specimen demonstrated poorly differentiated squamous cell carcinoma in the submucosa of the left upper lobe carina.

The diagnosis of bilateral simultaneous primary squamous cell carcinoma of the lung was made and the patient was treated with Chloromycetin for 2 weeks to improve the pneumonitis distal to the bronchial obstruction. A course of x-ray therapy was advised on an outpatient basis for palliative treatment. The possibility of pulmonary resection was discussed at some length but was thought inadvisable in view of the finding of tumor in the submucosa of both upper lobe carinas. It was felt that curative resection would not be feasible in this patient.

DISCUSSION

Bilateral simultaneous primary invasive squamous cell carcinoma of the lung diagnosed in a living patient is most unusual and has not been reported. Howard and Williams[1] recently described a patient with squamous cell carcinoma of the right main bronchus treated by pneumonectomy who had carcinoma in situ in the middle lobe and right lower lobe bronchus discovered by microscopic examination of the surgical specimen. This patient died on the twenty-fourth postoperative day from a bronchopleural fistula and empyema. Examination of the autopsy material demonstrated a small microscopic area of invasive squamous cell carcinoma at the junction of the left upper lobe and the left lower lobe bronchus. Other authors[2] have reported similar cases of squamous cell carcinoma of the lung, treated by pulmonary resection, in which a squamous cell carcinoma of the lung was detected years later in the opposite lung by follow-up x-ray studies or by examination of the autopsy material. The presence of carcinoma in situ in one lung when the other has been the site of invasive squamous cell carcinoma has been reported.[3, 4]

This case report is unique in that bilateral pulmonary neoplasms were encountered which simulated a chronic inflammatory process on initial examination. A bronchogram demonstrated abrupt segmental bronchial obstructions in both upper lobes suggesting a tumor as the most likely cause of this endobronchial abnormality.[5] Bronchoscopy and bronchial biopsy demonstrated squamous cell carcinoma in both the right and left upper lobe bronchi. The position of these tumors did not allow curative resection and treatment consisted of antibiotics to decrease pneumonitis. Palliative x-ray therapy was advised if further symptoms developed.

The possibility that one of these lesions could be a metastasis from the other side was considered but thought to be unlikely for several reasons: 1. Squamous cell carcinoma of the lung rarely, if ever, develops a solitary metastasis in the contralateral lung. 2. An abrupt endobronchial obstruction usually indicates the presence of a primary bronchogenic carcinoma.[5] 3. If one lesion represented metastasis by lymphatic extension, a positive bronchial biopsy would have been expected to show involvement of the submucosal lymphatics on the first examination. However, normal bronchial mucosa was obtained from both the right and left upper lobe bronchi at the time of the initial biopsy, indicating that submucosal spread of the tumor had not occurred across the carina to the opposite side.

The presence of bilateral, central pulmonary lesions with abrupt endobronchial obstruction and normal intervening bronchial mucosa certainly suggests the presence of bilateral, simultaneously occurring, primary squamous cell carcinoma of the lung.

SUMMARY

1. The case history of a patient with bilateral, simultaneous primary squamous cell carcinoma of the lung is presented.

2. Bronchography demonstrated bilateral bronchial obstruction suggesting malignancy rather than infection.

3. The diagnosis was substantiated by bronchoscopy and bronchial biopsies which showed the presence of bilateral invasive carcinoma of the lung in a living patient.

REFERENCES

1. Howard, S. A., and Williams, M. J.: Bilateral Simultaneous Occurrence of Primary Squamous-Cell Carcinoma of the Lung, Cancer 10: 1182, 1957.
2. Williams, M. J.: Extensive Carcinoma In Situ in Bronchial Mucosa Associated With Two Bronchogenic Carcinomas; Report of Case, Cancer 5: 740, 1952.
3. Ryan, R. F., and McDonald, J. R.: Bronchogenic Carcinoma With In Situ Carcinoma in Opposite Lung; Report of Five Cases, Proc. Staff Meet. Mayo Clin. 31: 478, 1956.
4. Black, H., and Ackerman, L. V.: Importance of Epidermoid Carcinoma In Situ in Histogenesis of Carcinoma of Lung, Ann. Surg. 136: 44, 1952.
5. Wilt, K. E., Andrews, N. C., Meckstroth, C. V., Molnar, W., and Klassen, K. P.: The Role of Bronchography in the Diagnosis of Bronchogenic Carcinoma, Dis. Chest 35: 517, 1959.

AN UNCLASSIFIABLE TUMOR OF THE ESOPHAGUS

A Case Report

Victor Hay-Roe, M.D., Rogers Lee Hill, M.D., and
W. Harold Civin, M.D., Honolulu, Hawaii

LANE[1] recently reported a series of cases of peculiar stromal change associated with squamous cell carcinoma. He reviewed no esophageal cases, but Stout and Lattes[2] discussed and illustrated 2 similar cases in the Armed Forces Institute of Pathology Fascicle on Tumors of the Esophagus. At about this time we were puzzling over an unusual esophageal lesion.

CASE REPORT

J. L. K., a 56-year-old Hawaiian man, was first seen in January, 1957, complaining of pain in the right side of his throat, progressive dysphagia, hematemesis, and marked loss of weight.

Past history revealed treatment for pulmonary tuberculosis from 1950 to 1955. He had also been treated for syphilis in the past.

Physical examination revealed a poorly-nourished man who showed evidence of recent weight loss. X-ray studies of the chest showed considerable interstitial fibrosis and extensive pleural thickening on the right side. Esophagoscopy disclosed a large necrotic mass of what appeared to be impacted food, 20 cm. from the incisors. Biopsies were reported as showing "sarcoma, type undetermined."

The patient was prepared for esophagectomy and, through an upper abdominal incision, the stomach and lower esophagus were mobilized. A right thoracotomy disclosed a lung densely adherent to the chest wall, and much bleeding was encountered in mobilizing it. The esophagus was freed and the tumor palpated within it, just inferior to the aortic arch. During the procedure, the blood continued to ooze profusely from the right thoracic cage and the patient required multiple transfusions. His blood pressure dropped progressively and became unobtainable in spite of ten pints of blood, several of which were pumped in under pressure, and it was thought that the surgery should be terminated as rapidly as possible. Since the tumor could be moved up and down within the esophagus and was attached by only a small pedicle, a longitudinal esophagotomy was made and the tumor extruded from the esophagus. The pedicle was less than 1 cm. in diameter and was attached just below the arch of the aorta. A segment of esophageal wall, 2 cm. in diameter, surrounding the base of the pedicle was excised and the esophagotomy and the chest were closed, with two chest drainage tubes inserted through separate stab wounds. These were connected to water-seal suction. No evidence of metastases was found during the procedure. At the termination of the surgery the blood pressure ranged from 40 to 60 mm. Hg systolic but, with transfusion of 1,500 c.c. of blood, it gradually returned to normal levels. The patient made an uneventful recovery.

From the Departments of Surgery and Pathology, The Queen's Hospital, Honolulu, Hawaii.
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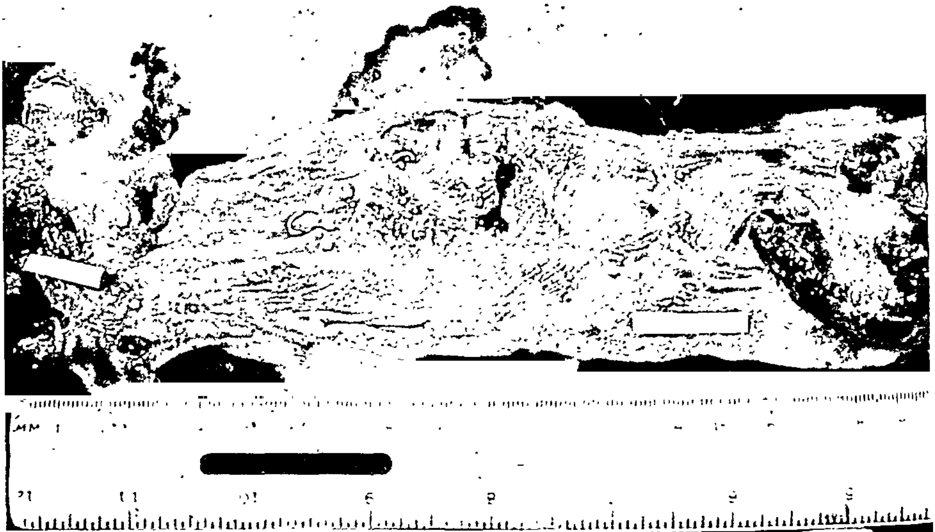
Pathologic Report (1).—The specimen consisted of an irregularly lobulated, ovoid, gray mass of soft tissue weighing 88 grams and measuring 10 cm. in greatest dimension. Microscopic examination revealed what was interpreted as a grade 2 leiomyosarcoma and a grade 3 squamous cell carcinoma (so-called collision tumor). This lesion was later reviewed and the possibilities of a leiomyoma with an associated squamous cell carcinoma, a carcinoma with pseudosarcomatous stromal alteration, or a carcinoma with areas resembling a sarcoma were also entertained.

Fig. 1.



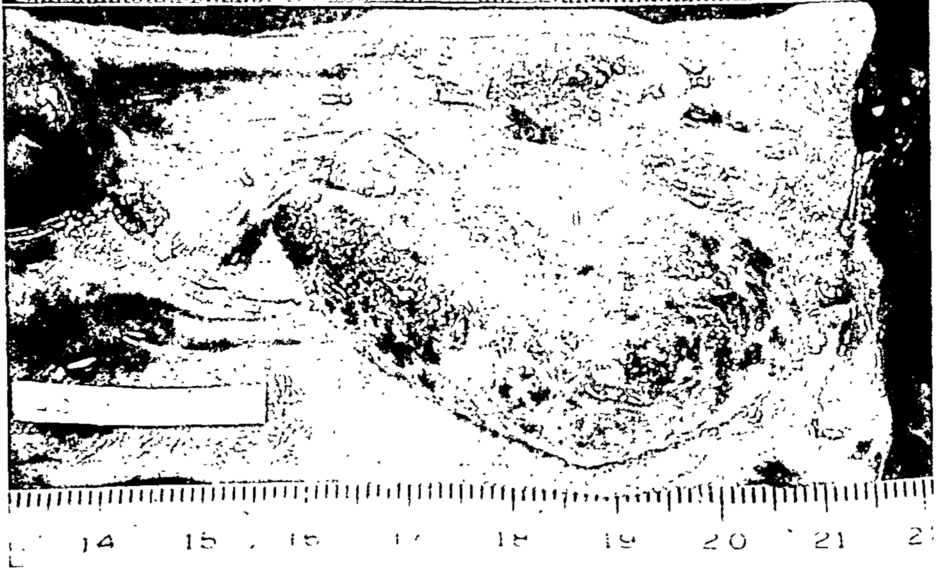


Fig. 2.

Fig. 1.—Resected segment of esophagus with sessile mass in the center and polypoid mass at one edge of the resection.

Fig. 2.—Close-up of polypoid mass near one edge of resection. The smaller polypoid mass extending from the base of the larger one can be seen above the large one in the photograph. At the left hand side of the photograph is a portion of the sessile mass.

The patient was ambulatory and able to eat soft foods on the fourteenth postoperative day, and he was discharged.

Because of the inadequacy of the surgery performed, the possibility of further surgery was suggested, but the patient refused. He gained weight and did fairly well for several months, but in January, 1958, he returned complaining of mild dysphagia and recent weight loss. Esophagograms at this time revealed two filling defects, one in the upper esophagus, the other just above the cardia. Esophagoscopy and biopsy proved the presence of recurrent tumor, and the patient then consented to further surgery (exactly 1 year following the first operation).

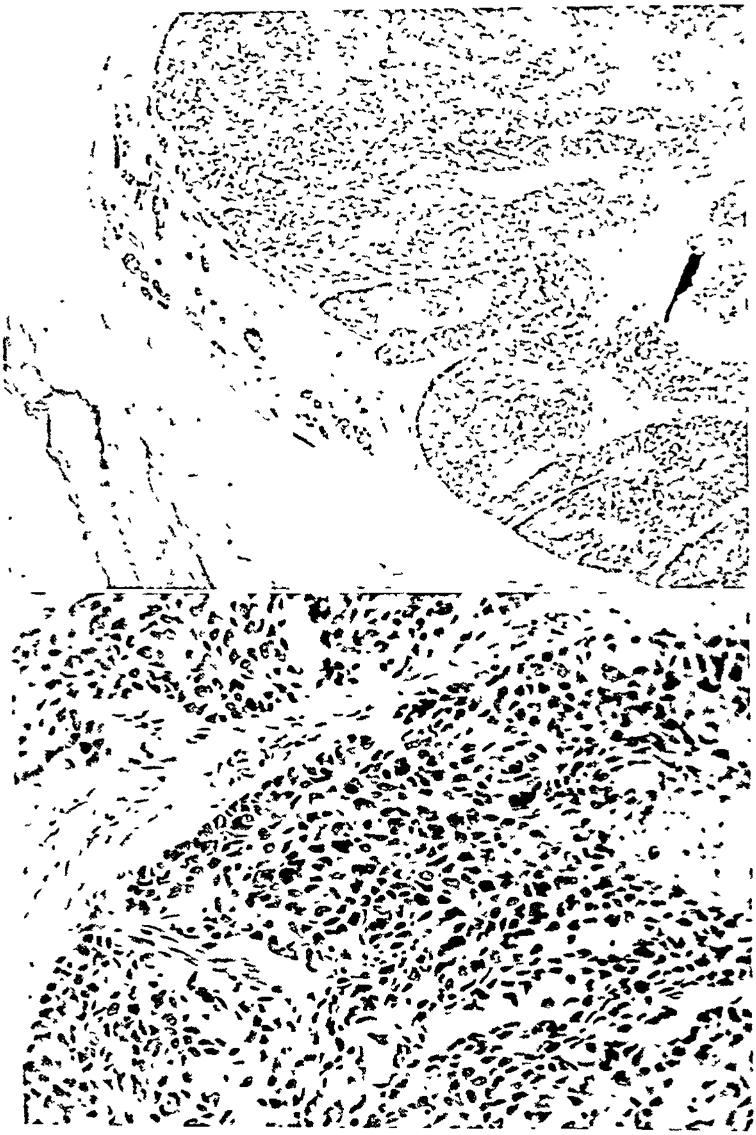


Fig. 3.—Photomicrograph showing masses of grade 3 squamous cell carcinoma invading esophageal wall. (Hematoxylin and eosin. *A*, ×45–*B*, ×265; both reduced ⅙.)

He was readmitted on Feb. 18, 1958, and a radical subtotal esophagectomy was carried out through the left chest, using a combined cervical, thoracic, and abdominal incision. The stomach and duodenum were mobilized and the gastric cardia was anastomosed to the remaining esophageal segment in the neck. Careful examination revealed one area in which the wall of the esophagus was indurated, but no spread through the wall could be detected. Critical exploration of the abdomen (including liver biopsy) and thorax revealed no evidence of metastases.

Pathologic Report (2).—The specimen consisted of a segment of esophagus measuring 21 cm. in length and weighing 105 grams (Fig. 1). Five centimeters from one end was a polypoid growth, 5 cm. in diameter (Fig. 2), which was attached by a narrow pedicle, approximately 1 cm. in diameter. At the base of this mass was another small pedunculated daughter growth, 1 cm. in diameter.

About 5 cm. from the other end, and extending to the mid-portion of the esophagus, was a sessile, nodular ulcerated growth which measured 1.5 to 2.5 cm. above the mucosa.

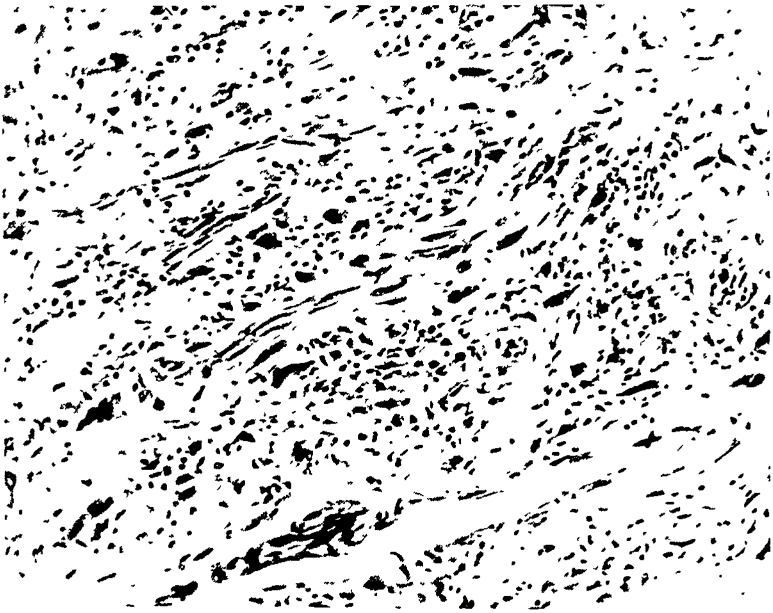


Fig. 4.—Medium-power view of anaplastic stromal giant cells (Hematoxylin and eosin ×265.)

Microscopically, the major part of the sessile tumor was composed of nests, masses, and columns of squamous cells (Fig. 3) with variably chromatic and pleomorphic nuclei, and cells showing anisonucleosis growing in the thickened submucosa and superficial muscularis propria. Where the mucosa was not ulcerated, the covering squamous epithelium was entirely normal and there was no evidence of surface origin of the lesion which appeared to have spread submucosally. No stromal change was seen. No lymphatic channels were noted to contain tumor emboli.

The pedunculated tumor and its offshoot were composed of a core of round and spindle-shaped cells with hyperchromatic oval nuclei. Cytoplasm was variable in amount, and cell membranes were often distinct, although at times indistinct. A large number of multinucleated giant cells (Fig. 4), not of the foreign body type, was present also. There was some infiltration by lymphocytes and plasma cells. The surface of the tumor was represented by a squamous cell carcinoma showing some superficial invasion and ulceration.

It is interesting to note that although known malignancy had been present for over a year at the time of the second operation, no metastases could be demonstrated. Even infiltration of the esophageal wall was not extensive. The lower mass may have been present, although certainly less extensive, at the first operation. However, it may not have been present then.

Following surgery the patient did poorly; he was dyspneic and slightly cyanotic with marked decrease in pulmonary capacity. He became rapidly worse and died on the first postoperative day. Death was probably a result of markedly reduced pulmonary capacity incident to an extensive fibrosis from an old tuberculosis.

DISCUSSION

This case illustrates an unusual esophageal tumor of a type which has been infrequently described in the literature. Lane,[1] in Stout's laboratory, reported several cases of similar tumor occurring in the mouth, pharynx, and larynx. These polypoid growths he designated as pseudosarcomas occurring in association with a squamous cell carcinoma. In his opinion, factors present in the connective tissue adjacent to a squamous cell carcinoma could stimulate the proliferation of connective tissue, resulting in a large polypoid growth with an inconspicuous squamous carcinoma at its base. He likens the proliferation of connective tissue to that seen following trauma or irradiation, as in the "granulation tissue sarcoma" mentioned by Ewing.[3]

There seemed to be four possibilities concerning the lesion in this case. It might have been (1) a carcinoma with pseudosarcomatous change in the stroma; (2) a malignancy of the collision type; (3) a carcinoma and a benign stromal tumor, as Pearlman[9] thought some so-called carcinosarcomas were, or (4) an anaplastic carcinoma. A check for myofibrils revealed none and many nuclei appeared adjacent to the extranuclear material and not surrounded by this, so we veered away from a diagnosis of leiomyoma.

The clinical course and apparent lack of metastases seemed against the diagnosis of anaplastic carcinoma. Also, because of lack of mitoses of the stromal elements and the rarity of occurrence, a malignant stromal tumor appeared unlikely. In favor of pseudosarcomatous change was the absence of deep invasion by the stromal element, although the squamous cell carcinoma extended into the muscle wall. Pseudosarcoma was also suggested by the ability of the tumor to propagate in tissue culture on numerous transplants as polygonal and spindle elements, depending on where the tissue was taken. These former cells also showed spindling of the edges of the transplants (Fig. 5). These constituents were maintained by reculture every week or so for a period of 5 months.

The emphasis placed on tissue culture in the diagnosis depends, of course, on one's teaching and experience. Autonomous growth, which this tumor displayed, is considered as a sign of malignancy by many; thus the stromal element might be considered as malignant. There is a marked tendency, however, for epithelial elements to spindle in tissue culture and this could be the explanation of the spindling.

Stout and Lattes[2] have illustrated 2 similar cases but made no conjecture as to the mechanism of development. The authors stressed confusing the lesion with sarcoma and they also stressed that an intramucosal and occasionally an invasive squamous cell carcinoma is always present.

A number of lesions called carcinosarcomas of the esophagus of polypoid character in the literature showed no metastases of stromal elements.[4-15] The possibility that some of these were carcinomas with pseudosarcoma has been entertained by both Stout and Lattes[2] and Lane.[1] Metastases occurred chiefly in polypoid lesions incompletely treated or of long duration, a point to be considered in the treatment of such lesions.

The question as to whether or not one can differentiate lesions in which the connective tissue element will metastasize from those in which it will not has not been resolved. Most such decisions would seem to be purely academic, because polypoid lesions with epithelial malignancy and stromal atypism, regardless of their origin, should be treated early and extensively since they often do not carry the dismal connotation of the usual squamous cell carcinomas of the esophagus. The usual squamous cell carcinoma ulcerates and infiltrates slowly although it gains access to lymphatics and metastasizes early. It does not give rise to symptoms until extensive infiltration of the esophageal wall (and often the adjacent mediastinal structures and lymph nodes) brings on dysphagia and weight loss. In contrast, the rarer group of malignancies represented by this case, by nature of their exophytic growth, usually cause dysphagia early and bring the patient to the physician while the lesion is still amenable to surgery. Furthermore, the intrinsic malignancy of the polypoid lesion appears less. Bad results seem to be related to inadequate treatment.

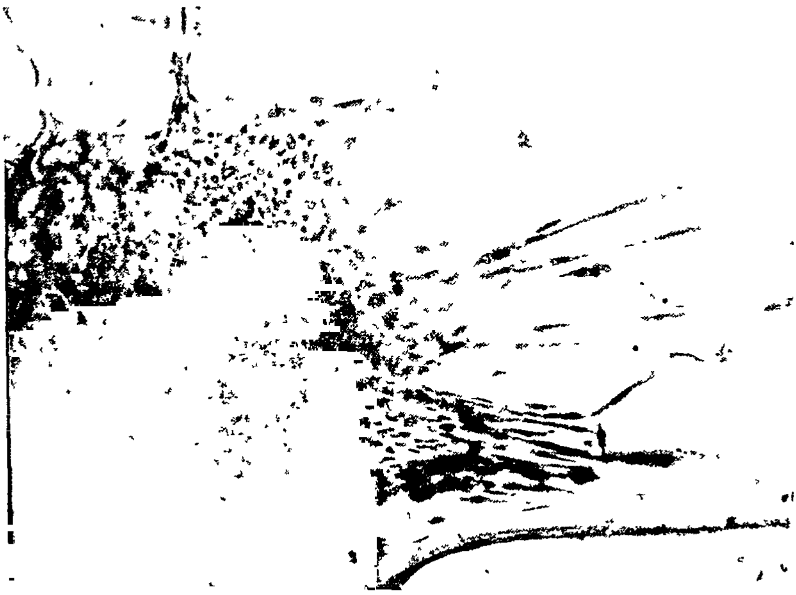


Fig 5—Photomicrograph of tissue culture growth in transplant which shows tendency of epithelial cells to spindle at the edges of the growth (Hematoxylin and eosin X120; reduced 1/6)

If, on biopsy of a polypoid tumor of the upper respiratory or digestive systems, a peculiar sarcoma-like (sometimes called sarcoma) proliferation of the stroma is noted, such a finding should alert the surgeon and the pathologist to the possible presence of an adjacent squamous cell carcinoma. Since the death of this patient the authors have been able to prove that such was the case in a tumor of the nasopharynx. An aggressive approach may be lifesaving.

SUMMARY

An unusual tumor of the esophagus, showing both epithelial and connective tissue elements and differing from the usual esophageal malignancy, is reported.

REFERENCES

1. Lane, N.: Pseudosarcoma (Polypoid Sarcoma-Like Masses) Associated With Squamous-Cell Carcinoma of the Mouth, Fauces and Larynx, Cancer 10: 19-41, 1957.
2. Stout, A. P., and Lattes, R.: Tumors of the Esophagus in Armed Forces Institute of Pathology: Atlas of Tumor Pathology, Washington, D. C., 1958, sec. V, fasc. 20.
3. Ewing, J.: Neoplastic Diseases: A Treatise on Tumors, ed. 4, Philadelphia, 1940, W. B. Saunders Company, pp. 223; 276-277.
4. Ackerman, L. V.: Surgical Pathology, St. Louis, Mo., 1953, The C. V. Mosby Company, pp. 267-268.
5. Ende, N., Pizzolato, P., Rader, L., and Ziskind, J.: An Unusual Case of the Carcinosarcoma of the Esophagus, Am. J. Roentgenol. 65: 227-231, 1951.
6. Gregg, J. B., and Stamler, F. W.: Unusual Neoplasms of the Esophagus, A. M. A. Arch. Otolaryng. 59: 159-169, 1954.
7. King, H. A., and Koerner, T. A.: Carcinosarcoma of the Esophagus, Surgery 42: 389-393, 1957.
8. Pearlman, S. J.: So-Called Carcinosarcoma of the Esophagus, Ann. Otol. Rhinol. & Laryng. 49: 805-820, 1940.
9. Poppens, A. D., Nicholas, A., and Szanto, P. B.: Carcinosarcoma of the Esophagus, Quart. Bull. Northwestern Univ. M. School 31: 271-277, 1957.
10. Scarff, G.: A Case of Carcinosarcoma of the Esophagus, J. Laryng. & Otol. 44: 324, 1929.
11. Smith, R., and Gowing, N. F. C.: Carcinoma of the Esophagus With Histological Appearance Simulating a "Carcinosarcoma," Brit. J. Surg. 40: 487-489, 1953.
12. Stout, A. P., Humphreys, G. H., II, and Rottenberg, L. A.: Carcinosarcoma of the Esophagus, Am. J. Roentgenol. 61: 461-469, 1949.
13. Thompson, J. R.: Carcinosarcoma of the Esophagus, J. THORACIC SURG. 25: 261-264, 1953.
14. von Hansemann, D.: Das gleichzeitige Vorkommen verschiedenartiger Geschwulste bei derselben Person, Ztschr. Krebsforsch. 1: 183, 1903-1904.
15. Warfield, C. L., and Darden, V. V.: Carcinosarcoma of the Esophagus, Bull. Georgetown Univ. M. Center 4: 71-75, 1950.

AN UNUSUAL VARIATION OF CONGENITAL TRACHEOESOPHAGEAL FISTULA

Case Report

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CONGENITAL anomalies can frequently be explained on the basis of known embryological development. Some of the more complex structural defects such as tracheoesophageal fistula, however, are not understood completely so that conjecture and surmise play important roles in ascertaining development. Despite lack of complete knowledge, a classification of known types of tracheoesophageal fistula has been accepted generally (Fig. 1). Variants from this grouping are uncommon. Such variants may sometimes corroborate previous ideas regarding development or they may confuse the situation further. The present report describes an interesting variation of tracheoesophageal fistula.

CASE REPORT

A male infant was delivered at another hospital on June 22, 1959, after a full-term, uneventful pregnancy. Labor and delivery were unremarkable. The mother was Rh negative, the father Rh positive, and the infant Rh negative. Two siblings were without congenital abnormalities.

During the first day of life, constant suctioning of the oropharynx was necessary because large amounts of mucus were produced which interfered with the airway. When the child was 12 hours old the diagnosis of esophageal atresia with probable tracheoesophageal fistula was made after appropriate radiological studies. Thoracic hemivertebrae were also demonstrated on these films. The child was transferred to this hospital where exploration was carried out through a right thoracotomy. Continuity of a dilated esophagus was noted. Dissection of the trachea from the esophagus revealed a fistula to be present between trachea and esophagus high in the chest at the thoracic inlet. This was divided in routine fashion and the trachea closed with some difficulty because of the location in the low neck. A tube passed from the nasopharynx could be palpated in the esophagus distal to the esophageal opening but could not be passed through the opening. Esophagostomy at a lower level was then performed and a second catheter passed from below. This catheter emerged through the previous fistulous connection with the trachea. It was then apparent that a septum was present which divided the esophagus with a fistulous connection to the trachea inferior to it. The esophagus was then opened in its mid-portion and the septum divided. The esophagostomy openings were closed.

The postoperative course was benign during the first few days after operation. Oral nutrition was started on the fifth postoperative day and went well for 24 hours. An episode of aspiration of a feeding occurred on the second day of feeding and severe pneumonitis

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developed. Feedings were continued, however, and were uneventful until the eighth postoperative day when another aspiration episode took place. Radiographic examination of the esophagus, using thin barium, was done and demonstrated patency of the esophagus with free flow to the stomach. Aspiration of barium occurred during the examination which outlined the trachea, demonstrating a possible fistula to the esophagus at the level of the first thoracic vertebra. A gastrostomy was then done for feeding purposes. The child took the nutrition per gastrostomy well for 9 days when another episode of aspiration occurred. Following this, the pneumonia became more marked and several episodes of cyanosis were noted.

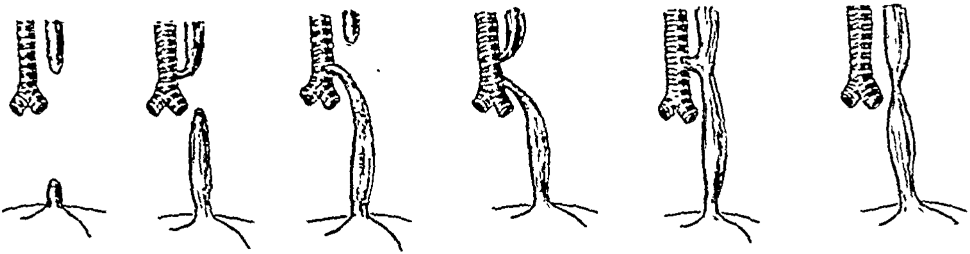

Fig. 1.—The common types of congenital abnormalities of the esophagus (from Gross[1]).

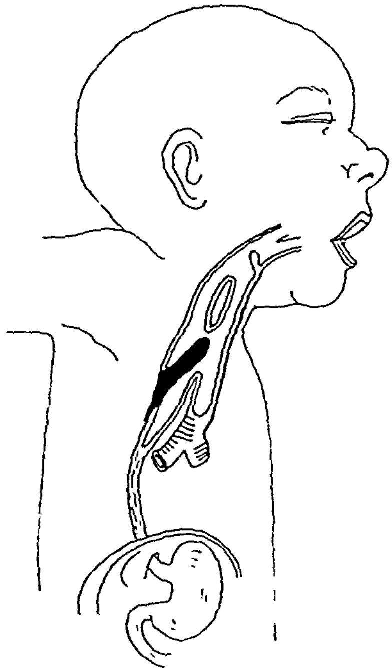

Fig. 2.—A diagrammatic representation of the patient reported here. The esophagus and trachea have been cut open to show the esophageal septum (solid black) and its relation to the fistulas.

The general condition of the child deteriorated. On the twenty-third day of life a cardiac murmur was heard for the first time and it was evident that congestive cardiac failure was present. Digitalis was given but rapid worsening in the child's condition followed and he died on the twenty-eighth postoperative day.

Postmortem examination revealed the area of repair to be intact without evidence of leak. Meticulous examination of the specimen revealed a second, minute tracheoesophageal fistula in the neck, about 1.5 cm. above the repaired one. This second fistula was so small as to have been overlooked during the preliminary appraisal of the organs (Fig. 2).

Marked hypertrophy of the right heart was present with interauricular and interventricular septal defects and a bicuspid aortic valve. Coarctation of the aorta and a patent ductus arteriosus were present, as was marked hydrocephalus.

Death was attributed to right heart failure. Acute cor pulmonale resulting from the marked pneumonia and consolidation of the lungs probably caused decompensation of the congenitally abnormal heart.

DISCUSSION

Unusual features in the patient presented here are (1) the septum in the esophagus associated with (2) the high location of the fistula to the trachea which was closed at operation and (3) the presence of a second tracheoesophageal fistula in the neck which was noted at autopsy. This infant resembled a child reported by Singleton and Knight[2] in whom two fistulas were present—the first repaired successfully, the second found in the neck at postmortem examination.

A review of the normal development of the trachea and esophagus offers some suggestions as to the development here. During the fourth week of gestation, the primordial respiratory tract anlage appears from the ventral side of the foregut. This outgrowth separates from the gut by the growth of bilateral longitudinal ridges which fuse. The fusion extends cranialward while the tracheal portion grows caudally rapidly. Some time before the seventh week of development it is believed that the esophageal lumen is obliterated by epithelial proliferation to recanalize during the eighth week. It is possible that the septum in the patient here represented a persistence of the obliteration of a segment of the esophageal lumen. Variation in growth rate of esophagus and trachea could account for the fistulas although it is difficult to explain the higher than usual location of them.

SUMMARY

A variation of congenital tracheoesophageal fistula has been presented in which there was esophageal continuity, a mid-esophageal septum, and two separate fistulas to the trachea. Autopsy following death on the twenty-eighth day of life disclosed additional abnormalities: hypertrophy of the right heart, interauricular and interventricular septal defects, bicuspid aortic valve, coarctation of the aorta, patent ductus, and marked hydrocephalus.

REFERENCES

1. Gross, R. E.: The Surgery of Infancy and Childhood, Philadelphia, 1953, W. B. Saunders Co.
2. Singleton, A. O., and Knight, M. D.: Congenital Atresia of the Esophagus With Tracheo-Esophageal Fistulae, Ann. Surg. 119: 556-572, 1944.

BRONCHOGRAPHY THROUGH PUNCTURE OF THE CRICOTHYROID MEMBRANE

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In view of the (1) inconsistent radiologic results, (2) toxic anesthetic reactions, (3) technical difficulties, and (4) discomfort to the patient following any of the laryngeal catheterization methods by the oral or nasal route, it was decided to evaluate the method of bronchography, as originally suggested by Sicard and Forestier in 1922, which has been used much more frequently on the continent and in England than in this country. Numerous advantages and disadvantages appeared to us in our review of the literature and in our original consideration of this technique. The advantages appeared to be that, without the irritating presence of a catheter, the amount of local anesthetic necessary would be greatly reduced since only the subglottic portion of the tracheobronchial tree would require anesthesia. This in turn should decrease the number of toxic reactions as well as increasing the patient comfort and safety. Since the cough reflex as initiated by laryngeal and carinal stimulation was eliminated, it was believed that more constant radiologic results could be obtained. Technically the necessary positioning of the patient during the procedure, in order to obtain complete segmental filling, appeared to us to be a possible inherent weakness in this technique. Other disadvantages considered were the possibility of damage to the trachea, perforation of the esophagus, extravasation of the dye into the paratracheal tissues, the possibility of subcutaneous and mediastinal emphysema and infection, air embolism, or breakage of the needle in the trachea.

HISTORICAL DATA

Bronchography was originally performed by Chevalier Jackson[1] in 1905 by means of insufflation of a bismuth subcarbonate compound through the bronchoscope. Sicard and Forestier[2] reported the use of Lipiodol by means of cricothyroid puncture in 1922. Numerous other technical methods have been used for the introduction of the bronchographic medium; the introduction of the nasal catheter into the trachea under topical anesthesia has been the most

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widely used method in the United States. Due to its slow absorption and possibility of tissue reaction, Lipiodol has now been supplanted, first, by a partial transition to the water-soluble bronchographic compounds which were not completely satisfactory, and now to Dionosil which is an aqueous or oily suspension of a salt of the basic same acid as Diodrast. When warmed it has offered a medium of low irritation, good contrast, satisfactory viscosity, and disappears from the lungs within 24 hours. The choice of the topical anesthetic has changed from the use of cocaine originally to a now wide variety of potent agents of low toxicity. Both Xylocaine and Cyclaine were used satisfactorily during this study. The bronchopulmonary segmental anatomic terminology, as suggested by Jackson and Huber[9] in 1943, was used for conformity in this study since the patients investigated represented the combined therapeutic problems of the medical, radiologic, anesthetic, and surgical teams.

INDICATIONS

The chief value of bronchography lies in the demonstration of the presence or absence of bronchiectasis. Its use, we believe, should not be restricted to those patients with the typical symptomatology of a cough productive of large amounts of sputum but should be given serious consideration in all cases of hemoptysis as an adjunct to other more commonly used methods of diagnosis to eliminate the possibility of unsuspected upper lobe involvement in the presence of a normal routine chest film. Its use as a guide in the surgical treatment of pulmonary tuberculosis is becoming a more widespread feature. Rare congenital abnormalities, as well as foreign bodies and tumors of the bronchus, may on occasion be diagnosed only by the performance of bronchography. The etiology of pulmonary cysts may also be ascertained, and other diseases, such as asthma and emphysema, may show not only slight morphologic changes but also changes in bronchophysiologic characteristics. Since we believe this to be a procedure which offers a good percentage of useful yield with low morbidity, the variety of clinical problems as mentioned above are considered indications for bronchography.

TECHNIQUE

Premedication in these cases has varied with the use of either a barbiturate 90 minutes before the procedure combined with morphine and atropine 60 minutes before the procedure as the standard, with use of the barbiturate or narcotic alone, or no premedication in certain individual cases. The former patients naturally were less apprehensive, with slightly diminished secretions and cough reflex. The personality make-up of the individual seemed to be as important as any factor in determining the difference between a very cooperative and comfortable patient and the small percentage of others who were not. A complete and thorough explanation of the procedure appears to be of the utmost importance in obtaining patient cooperation. The patient is positioned with the head slightly extended on the fluoroscopic table with the head of the table elevated approximately 20 degrees. The area is prepared, using Phisohex and aqueous Zepharin. Local anesthesia of the skin and cricothyroid membrane is obtained by either 1 c.c. of 1 per cent Cyclaine or 1 per cent Xylocaine. Following this, a 16-gauge needle specially prepared with a short bevel, and of a length calculated to penetrate one half of the diameter of the trachea from the skin, is inserted. Flexible polyethylene tubing is then connected to the needle and approximately 2 c.c. of 1 per cent Cyclaine is injected with the patient on his back, and 1 c.c. with the patient on his right side and 1 c.c. when on his left side. (In only one instance, early in our performance of this technique, was it necessary to reinsert the needle because of the vigorous swallowing of the patient.) After this procedure the patient is allowed to rest for several minutes before, under intermittent fluoroscopic control, 15 c.c. of warmed aqueous or oily Dionosil is injected with the patient on his back and then another 5 c.c. with the patient lying on his right side, having turned approximately 120 degrees, then back on his left side through the same arc for another injection of 5 c.c. Filling is checked and, if satisfactory, films are taken at a target—film distance of 6 feet. If any segment is not filled satisfactorily he is positioned properly and another 5 c.c. is injected before completion of fluoroscopy. After these films are viewed the patient is asked to breathe deeply and cough gently several times before the final posteroanterior film is taken. We have found that on occasions this will provide somewhat of a more definite air contrast coating of the bronchi without appreciable alveolar filling. The needle is removed and a small Band-aid dressing is applied which is removed in 24 hours.

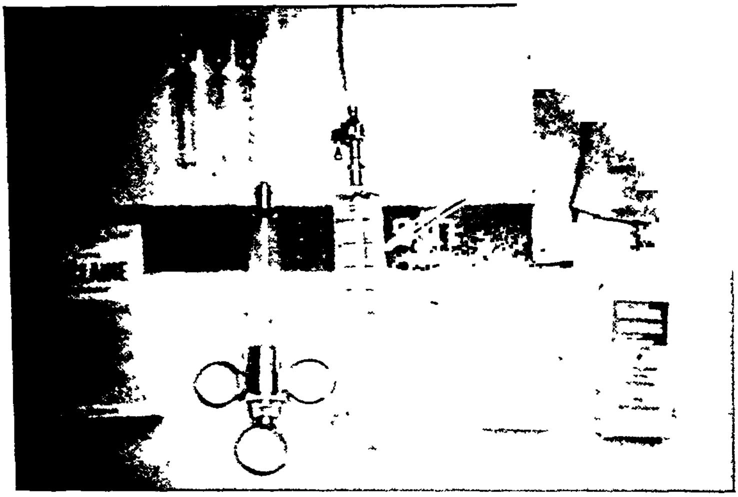


Fig 1.—Bronchographic materials

RESULTS

During the period of study, seventeen bronchograms were performed by the laryngeal catheterization method using the same type of premedication and anesthetic agents, except that with the latter cases, even when an aersol was used, anesthesia was never completely satisfactory using less than 12 c.c of 1 per cent Xylocaine or 1 per cent Cyclaine, and it usually required slightly more (This is in comparison with an average of 5 c.c. when using the cricothyroid puncture technique.) In the 17 catheterization cases, there was one convulsive reaction, 1 patient with transient cyanosis, and 3 patients with mild reactions of pallor, sweating, bradycardia, and hypotension. Ninteen cricothyroid membrane puncture bronchograms were performed with the technique

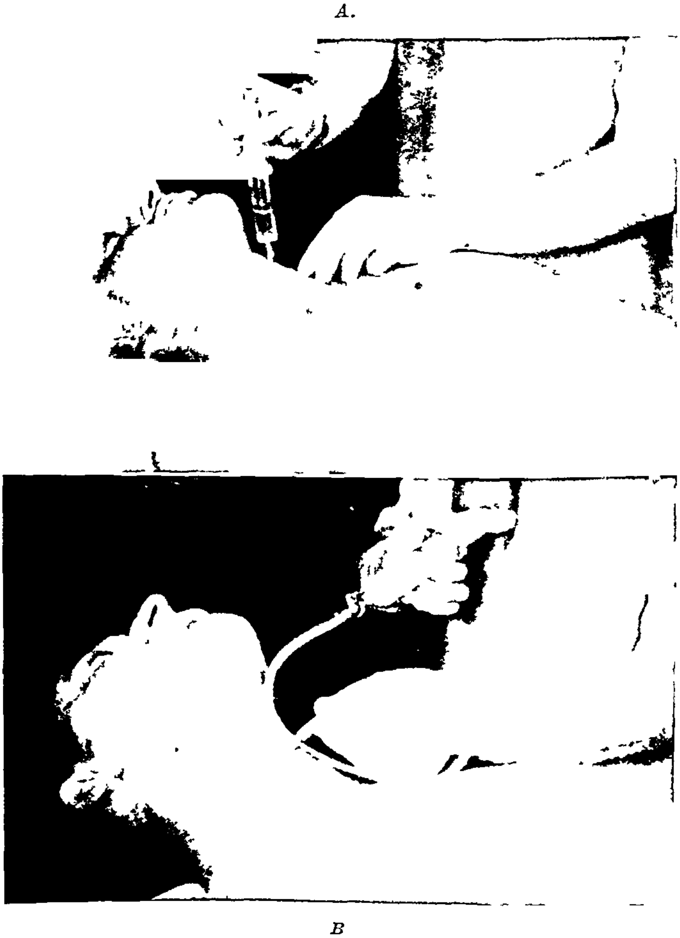
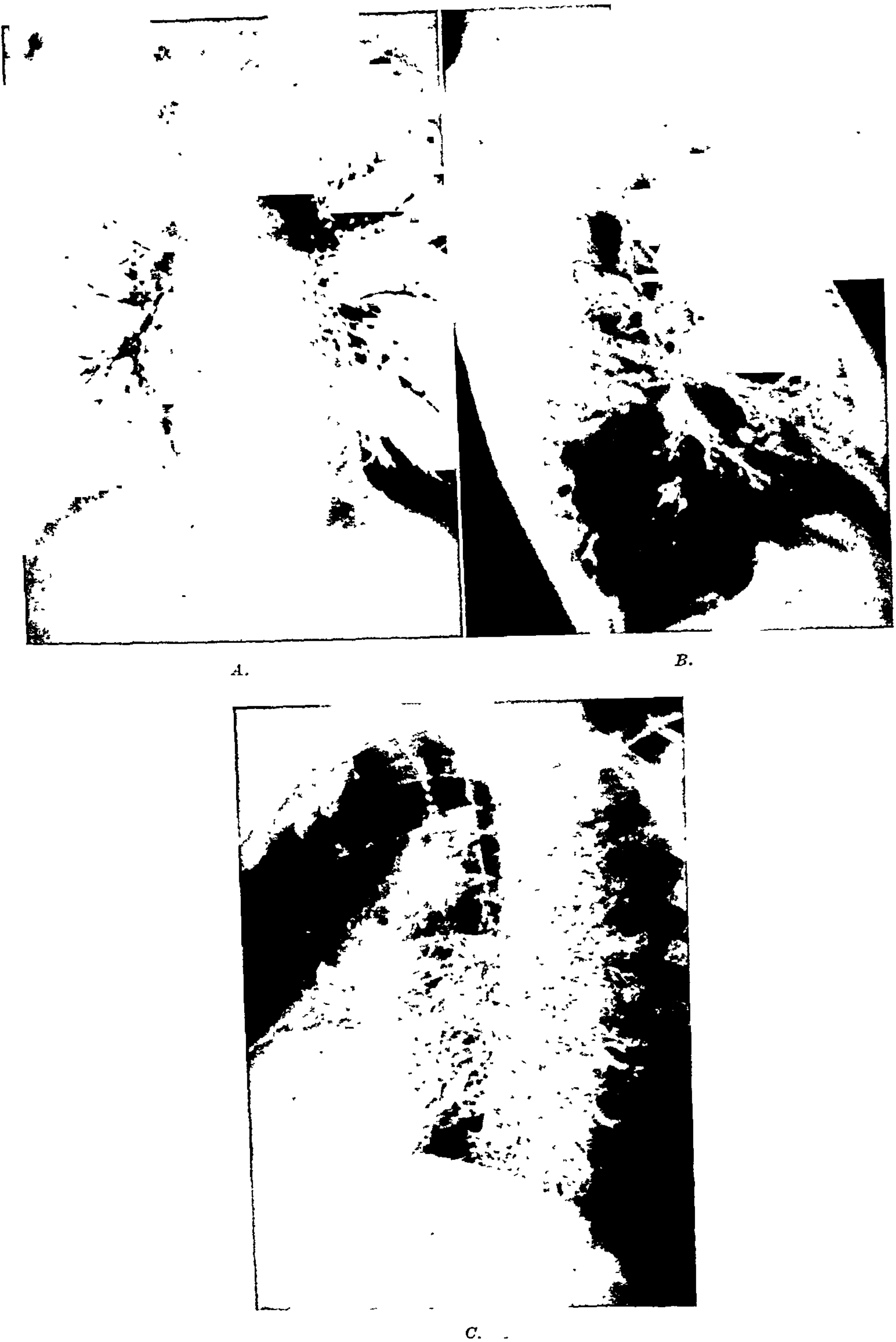


Fig. 2.—Bronchographic technique *A*, Insertion of local anesthesia *B*, Injection of the bronchographic medium

outlined previously with only one instance of syncope and bradycardia in this group. In an evaluation of the diagnostic quality of the films, it was considered that there was incomplete filling in 4 of the 17 cases in the first group, whereas, in the latter, there was only 1 case in which the filling was not completely satisfactory. The over-all quality was much better in the group which had had cricothyroid membrane puncture. As far as patient comfort was



A.

B.

C.

Fig. 3.—Representative bronchograms. *A*, R.N. (No. 26501). An anteroposterior view which shows bronchiectasis of the basilar segments of the left lower lobe. *B*, A.K. (No. 24219). A lateral view which shows bronchiectasis of the middle lobe and basilar segments of the right lower lobe. *C*, M.G. (No. 25512). A right anterior oblique view which shows extensive basilar segmental bronchiectasis.

concerned, 5 patients of the second group had previously had laryngeal catheterization bronchography and all 5 expressed strong preference for the needle method. Technically, by using the method described, there was less difficulty in filling the upper lobes through the needle than had been anticipated, although the head of the table was never lowered below 10 degrees above the horizontal. There was 1 patient in whom the needle did slip out of the trachea near the end of the procedure resulting in a minimal extravasation which cleared spontaneously in 72 hours. One patient developed a nonhemolytic streptococcal cellulitis surrounding the site of the needle puncture and the same organism was cultured from the tracheobronchial tree. This responded well to appropriate antibiotic therapy and warm compresses but did prolong his hospital stay for several days beyond that which would have been required for the completion of his diagnostic workup. (Several of the films and a picture of the material necessary for the performance of this type of bronchography are included.) It is our belief that the use of a number of short beveled needles of various lengths, so that one can be chosen of the correct length to measure just that distance between the skin and the mid-diameter of the trachea, is a very important factor in the prevention of complications in this technique.

DISCUSSION

In a comparison of our limited series of patients between the nasal catheterization method with the cricothyroid puncture method, we were impressed with the advantages of the latter. In the group which had catheterization there was one convulsive reaction which responded well to an intravenous barbiturate and oxygen, and one episode of transient cyanosis. Three patients showed milder reactions of pallor, sweating, bradycardia, and hypotension, whereas, in the cricothyroid group there was only 1 case of bradycardia and hypotension which cleared spontaneously.

In the group with cricothyroid puncture, there was 1 case of minimal extravasation and 1 other in which a cellulitis developed around the injection tract which required treatment and prolongation of the hospital stay for several days.

Taking all factors into consideration, it was our belief that the latter procedure was the most satisfactory because of its decrease in anesthetic reactions and its overwhelming preference by the patients, particularly those on whom the catheterization method had been used previously. Its simplicity and ease of performance, combined with the production of much more satisfactory diagnostic films, are additional assets to be considered in the choice of methods. Our hope is that this method will be given a more widespread trial in the United States than it has had, in order to ascertain if the disadvantages mentioned earlier might not be more rare than originally anticipated.

the transtracheal method, as described by Sicard and Forestier in 1922 and used more generally on the continent and in Great Britain than in the United States.

The patient is prepared for this procedure by a combination of morphine and atropine given 1 hour before the procedure with a barbiturate sometimes added, although the technique has been satisfactorily performed with no premedication. The patient is positioned on the fluoroscopic table with the neck slightly hyperextended. Local anesthesia is obtained by a total dose of 5 c.c. of the anesthetic solution (1 per cent Cyclaine or Xylocaine) and the bronchographic medium is injected through a 16 gauge needle which has been inserted through the cricothyroid membrane. It is of importance that this needle be of such length as to approximate the distance between the skin and the mid-diameter of the trachea. Dionosil is used as the bronchographic medium and bronchial filling of all segments is accomplished by positioning of the patient, being careful not to lower the head more than 10 degrees in order to prevent reflux into the unanesthetized larynx.

In evaluating this method, bronchoscopy performed by catheterization was compared with that performed transtracheally, with the latter method being the more satisfactory in our hands in alleviating the difficulties mentioned. It is hoped this technique will now be given a more widespread trial to ascertain its true place in our diagnostic armamentarium.

REFERENCES

1. Jackson, C.: The Bronchial Tree; Its Study by Insufflation of Opaque Substances in the Living, Am. J. Roentgenol. 5: 454-455, 1918.
2. Sicard, J. A., and Forestier, J.: Methods générale d'exploration radiologique par l'huile iodée (Lipiodol), Bull. et mém. Soc. d. hôp. de Paris 46: 463-469, 1922.
3. Guy, J., and Elder, H. C.: Preliminary Report on Radiographic Exploration of Broncho-Pulmonary System by Means of Lipiodol, Edinburgh M. J. 33: 269-273, 1926.
4. Leroux, L., and Bouchet, M.: Sur les accidents des injections intra tracheales, Rev. Laryngol. 47: 360-365, 1926.
5. Olmer, D., and Zuccoli, G.: Accidents nerveux subitis épileptriformes au cours d'une injection intratrachéale de Lipiodol, Paris méd. 2: 306-307, 1929.
6. Kohler, B.: Eine missgluckte bronchographie, Acta radiol. 13: 54-56, 1932.
7. Hart, F. D.: Positioning in Bronchography, Brit. M. J. 2: 7-8, 1942.
8. Field, C. E.: Bronchography in Children, Lancet 2: 357-359, 1942.
9. Jackson, C. L., and Huber, J. F.: Correlated Applied Anatomy of the Bronchial Tree and Lungs With a System of Nomenclature, Dis. Chest 9: 319-326, 1943.
10. Schmidt, H. W.: A Method of Obtaining Bilateral Bronchograms, Proc. Staff Meet. Mayo Clin. 23: 71-77, 1948.
11. Vickers, A. A.: Bronchography. Methods by Which It May Be Performed and Factors Influencing the Choice of the Method Employed, Brit. J. Radiol. 22: 137-151, 1949.
12. Rienzo, S. D.: Radiologic Exploration of the Bronchus, Oxford, Blackwell Scientific Publications, and Springfield, Ill., 1949, Charles C Thomas, publisher.
13. Millder, J. B., Conyars, W. H., Jr., and Dinhoffer, N.: A Single Safe Bronchographic Technique for Children, J. Pediat. 36: 721-727, 1950.
14. Shanks, S. C., and Kerley, P., editors: A Textbook of X-ray Diagnosis by British Authors, Philadelphia, 1950, W. B. Saunders Company, pp. 311-314.
15. Buckes, M. G., Potts, W. L., Davidson, H. B., and Neptine W. B.: Bronchography in Pulmonary Tuberculosis, Am. Rev. Tuberc. 64: 394, 1951.
16. Don, C.: A New Medium for Bronchography, Brit. J. Radiol. 25: 573-578, 1952.
17. Sadove, M. S.: Classification and Management of Reactions to Local Anesthetic Agents, J. A. M. A. 148: 17, 1952.
18. Orkin, L. R., and Rovenstine, E. A.: Hexylcaine (Cyclaine): Usefulness in Regional and Topical Anesthesia, Anesthesiology 13: 465, 1952.
19. Holden, W. S., and Crone, R. S.: Bronchography Using Dionosil Oily, Brit. J. Radiol. 26: 317-322, 1953.

20. Crawford, O. B.: Comparative Qualities of Three New Local Anesthetic Drugs: Xylocaine, Cyclaine, and Pravocaine, Anesthesiology 14: 278, 1953.
21. Flipse, M. E., Hedberg, G. A., and Kruger, V. R.: Water-Soluble Contrast Medium for Bronchography, A. M. A. Arch. Otolaryngol. 57: 188-205, 1953.
22. Peck, M. E., Noerkan, A. J., and Salzman, E.: Clinical Experience With the Water Soluble Bronchography Compounds, J. THORACIC SURG. 25: 234-245, 1953.
23. Diehl, K. L.: Bronchography, A Study of Its Techniques and the Presentation of an Improved Modification, A. M. A. Arch. Otolaryngol. 60: 277-290, 1954.
24. Schmidt, H. W., and Donoghue, F. E.: The Techniques and Applications of Bronchography, Med. Clin. North America, p. 1207 (July), 1954.
25. Wisoff, C. P., and Felson, B.: Bronchography With Oily Dionosil, J. THORACIC SURG. 29: 435-446, 1955.
26. Phillips, F. J., Lalli, A., and Butler, W.: Bronchographic Studies as a Guide to the Surgical Treatment of Pulmonary Tuberculosis, J. THORACIC SURG. 32: 820-826, 1956.
27. Hewlett, J. H., Puglisi, A. J., and Bowers, W. F.: Bronchospasm in Bronchography, J. THORACIC SURG. 33: 609-616, 1957.
28. Haidak, G. L., Caplan, B., and Maloney, W. H.: Air Contrast Bronchography, J. THORACIC SURG. 34: 63-66, 1957.
29. Beck, R. E., and Hobbs, A. A., Jr.: A Technique for Bronchography, Am. J. Roentgenol. 79: 269-271, 1958.
30. Wilson, J. K. V.: Cricothyroid Bronchography With a Polyethylene Catheter, Am. J. Roentgenol. 81: 305-311, 1959.

ERRATUM

The dates of the next meeting of The American Association for Thoracic Surgery were erroneously given on the cover of June Issue as May 24, 25, and 26, 1961, instead of *April* 24, 25, and 26, 1961.

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Members Deceased

A. T. Bazin
Richard H. Dieffenbach
Aaron Himmelstein
William L. Keller
Victor O. Mader
Julian A. Moore
Edward J. O'Brien

ANNUAL MEETING NOTES

The Fortieth Annual Meeting of The American Association for Thoracic Surgery was held in Miami Beach, Florida, May 11, 12, and 13, 1960 There were 892 physicians who registered for the scientific sessions In addition there were 109 wives present The representation from foreign countries was rather impressive, particularly from the Far East

The meeting arrangements were satisfactory except for an unavoidable and incomprehensible mismanagement of the hotel reservation arrangements at The Deauville, as well as their satellite and supporting institutions along the Beach

As a result of extended deliberations over several years, by the Council, by special committees, as well as the Executive Session and the voting membership, the following proposals affecting the membership structure of the Association and embodying changes in the Constitution as well as the By Laws were adopted after due process

CONSTITUTION. ARTICLE III MEMBERSHIP

Former.—"*Section 1*—There shall be four classes of members. Active, Associate, Senior, and Honorary Admission to membership in the Association shall be by election There shall be no numerical limits on any class of membership Only Active and Senior members shall have the privilege of voting or holding elective office"

Adopted—"*Section 1*—There shall be four classes of members. Active, Associate, Senior, and Honorary. Admission to membership in the Association shall be by election Membership shall be limited, the limits on the respective classes to be determined by the By Laws Only Active and Senior members shall have the privilege of voting or holding elective office"

Former—"*Section 2*—Election to all classes of membership shall be for life, subject to the provisions of Section 3, following."

Adopted—"*Section 2*—Election to Active, Senior, and Honorary Membership shall be for life, subject to the provisions of Section 3, following After the 1960 Annual Meeting of the Association election to Associate Membership shall be for a limited period of time, as determined by the By Laws During this limited period, an Associate Member, if properly qualified, may be elected to Active Membership At the expiration of this limited period, an Associate Member, if not yet qualified for Active Membership, must either be reelected to an additional period of Associate Membership, or be dropped from the rolls of the Association."

Section 3. Unchanged.

BY LAWS: ARTICLE III

Former.—"*Section 2*—There shall be no numerical limit on Active Membership The candidate, to be eligible, must be a citizen of the United States of America or of Canada, unless in unusual cases this citizenship requirement shall have been waived by the Council The candidate shall have achieved distinction in the thoracic field, or shall have made a meritorious contribution to knowledge pertaining to thoracic disease or its surgical treatment

Under usual circumstances, Active Members shall be elected from the Associate Members who have satisfied all requirements for Active Membership. Under unusual circumstances, Active Membership may be awarded to new candidates of outstanding distinction."

Adopted.—"*Section 2.*—Active Membership shall be limited to three hundred fifty." (The remainder of the Section unchanged.)

Former.—"*Section 3.*—There shall be no numerical limit on Associate Membership. The candidate, to be eligible, may be a citizen of any country. All candidates for Associate Membership shall be engaged actively in the practice of clinical medicine, or in teaching, or investigative work in the basic sciences underlying clinical practice, and all shall have demonstrated an active interest in thoracic disease. In the case of those who are engaged in the independent practice of thoracic surgery, it shall be required that they present evidence of sound basic training in general as well as thoracic surgery. Clinicians of outstanding ability, whose interest is limited to a small fraction of the entire thoracic field, may be elected to Associate Membership."

Adopted.—"*Section 3.*—There shall be no numerical limit on Associate Membership. The candidate, to be eligible, may be a citizen of any country. All candidates for Associate Membership shall be engaged actively in the practice of clinical medicine, or in teaching, or investigative work in the basic sciences underlying clinical practice, and all shall have demonstrated an active interest in thoracic disease. In the case of those who are engaged in the independent practice of thoracic surgery, it shall be required that they present evidence of sound basic training in general as well as thoracic surgery. Clinicians of outstanding ability, whose interest is limited to a small fraction of the entire thoracic field, may be elected to Associate Membership. The limited period of time for Associate Membership, as required by ARTICLE III, *Section 2*, of the Constitution, shall be five years."

A change which would limit the number of visitors at each meeting was defeated. Thus, the scientific sessions still remain open to those interested and qualified physicians who register in appropriate manner.

The following changes in membership status were approved by the Council and passed by the membership in Executive Session:

Four members were dropped from the rolls of the Association either through the acceptance of their resignations or because of nonattendance.

The following Active members were elevated to Senior status:

J. Dewey Bisgard
Joseph W. Gale
Ernest C. Janes
Clarence A. McIntosh
James L. Mudd
George F. Skinner
George Willauer

The following Associate members were elevated to Active membership:

Thomas G. Baffes
James S. Battersby
Philip E. Bernatz
William S. Blakemore
Ivan W. Brown, Jr.
John C. Callaghan
E. Stanley Crawford
John F. Dammann, Jr.
Julio C. Davila
William W. Heroy
Charles A. Hufnagel
Karl E. Karlson
Harvey W. Kausel
John Lester Kee, Jr.
James Alastair Key
Earle B. Mahoney
Elliott Michelson
Peter V. Moulder
Thomas F. Nealon, Jr.
David C. Sabiston, Jr.
Frank C. Spencer
Lawrence H. Strug
Frederick H. Taylor
William I. Wolff

The following candidates were elected to Associate membership:

Jesse E. Adams, Jr., Chattanooga, Tenn.
Murray N. Andersen, Buffalo, N. Y.
John E. Connolly, San Francisco, Calif.
Milton V. Davis, Dallas, Texas
Hugh F. Fitzpatrick, New York, N. Y.
Joseph J. Garamella, Minneapolis, Minn.
John P. Heaney, San Antonio, Texas
Robert H. Holland, Dallas, Texas
James B. Littlefield, Charlottesville, Va.
Daniel E. Mahaffey, Louisville, Ky.
Charles V. Meckstroth, Columbus, Ohio
Fletcher A. Miller, Minneapolis, Minn.
Thomas C. Moore, Indianapolis, Ind.
Edward R. Munnell, Oklahoma City, Okla.
Joseph W. Peabody, Jr., Washington, D. C.
Robert G. Pontius, Pittsburgh, Pa.
George Robinson, Mount Vernon, N. Y.
Dennis M. Rosenberg, New Orleans, La.
Robert J. Schramel, New Orleans, La.
Thomas W. Shields, Chicago, Ill.
Harold C. Spear, Miami, Fla.
Warren J. Taylor, Boston, Mass.
Milton Weinberg, Jr., Evanston, Ill.
William Glenn Young, Jr., Durham, N. C.

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PRESIDENTIAL ADDRESS

PULMONARY RESERVE AND ITS INFLUENCE ON THE DEVELOPMENT OF LUNG SURGERY

William E. Adams, M.D., Chicago, Ill.

Members of the American Association for Thoracic Surgery and Guests:

I wish to begin this discussion by expressing my deep appreciation for the high honor of being chosen to serve as President of our Association. I first attended a meeting of this distinguished Society in 1929. The meeting was held at Barnes Hospital, St. Louis, in a medium-sized classroom. During the 31 intervening years, thoracic and cardiovascular surgery has grown and matured, and our organization has continued to enjoy an enviable reputation among graduate medical educational groups.

During my 25 years of membership, I have attended all annual meetings except one, at which time I was doing graduate work under Prof. Ferdinand Sauerbruch at the University of Berlin. My experiences during these years, in listening to the presentations, in occasional participation in the programs, and in enjoying the general fellowship of this Association, are among the most treasured memories of my professional career.

I would like at this time also to express my appreciation to the other officers and councilors of the Association for their valued counsel, and especially to thank our Secretary, Dr. Langston, and our Administrative Assistant, Miss Hanvey, who have handled the many and varied affairs of our Society in a most expert and proficient manner.

From the Department of Surgery, University of Chicago, Chicago, Ill.

Presented at the Fortieth Annual Meeting of The American Association for Thoracic Surgery at Miami Beach, Fla., May 11-13, 1960

In deciding upon a subject for this occasion, various educational, historical, and scientific problems presented themselves. Provocative questions were not lacking in any of these areas. The subject I have chosen is one that first interested me over two decades ago at the time of several deaths following total pneumonectomy. Autopsy findings in these cases were those of cardiac failure, although no primary cardiac lesion was found. At that time, total pneumonectomy was the only curative type of surgery considered for primary carcinoma of the lung.

Although much concern regarding pulmonary function and reserve was expressed in early medical history, the full significance of this matter was not appreciated until the years of development of modern thoracic surgery. The delay in an understanding of this problem was due partly to the difficulty in evaluating pulmonary reserve, which later was forced upon us (partly by trial and error) with the evolution of modern pulmonary surgery. It is now appreciated that this problem is not confined only to pulmonary resection, but also to other intrathoracic surgery, as well as in the general field of surgery, especially in the elderly or poor-risk patient. Interference with pulmonary ventilation following a general anesthetic and major operation in the older age group, or in the obese patient, tends to encourage the retention of bronchial secretions with resultant patchy atelectasis. This in turn may lead to increased pulmonary vascular resistance, as well as to hypoxia, which results in increased strain on the right heart. Evidence that this occurs quite frequently was demonstrated repeatedly in a study of a series of 50 patients who had undergone major surgery. The average level of arterial blood oxygen on the first

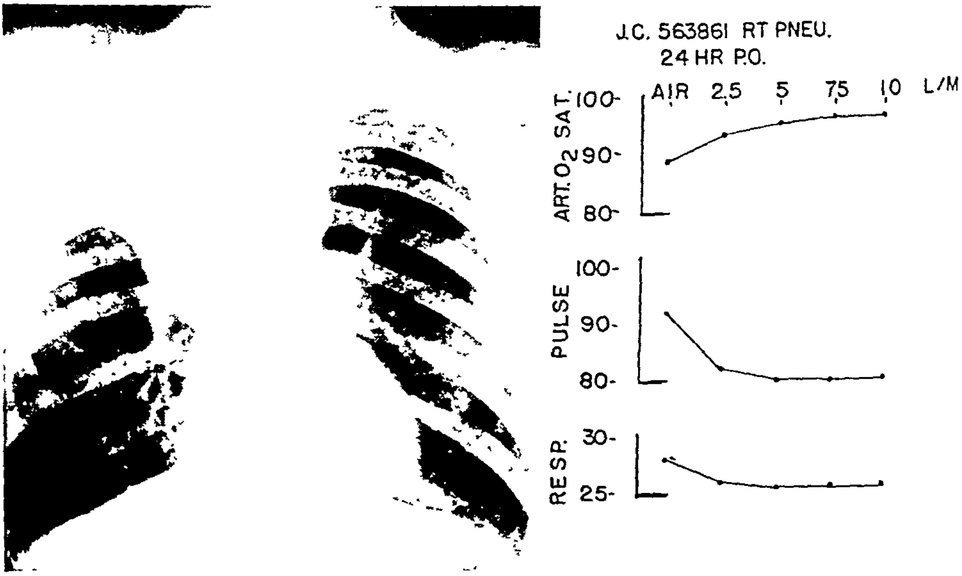


Fig. 1.—Roentgenogram of chest of a 63-year-old white man and data showing degree of desaturation of blood oxygen 24 hours following a right pneumonectomy. A satisfactory rise in arterial oxygen saturation was obtained by the administration of only 2½ L. per minute of oxygen flow via an oropharyngeal catheter. Note changes in pulse and respiration closely following the changes in arterial oxygen saturation.

day after operation was 88 per cent as seen in Fig. 1, with a range of 80 to 92 per cent. This could be readily corrected by the use of small amounts of oxygen administered through an oropharyngeal catheter. As little as 1 to 2 L. of oxygen flow per minute usually led to a desirable level of blood arterial oxygen. In the series of patients studied, some degree of hypoxia of clinical significance usually persisted for several days after surgery, the amount gradually decreasing as the patient became more active.[1]

The dangers accompanying decreased pulmonary reserve were recognized by the ancient Greeks. However, they understood relatively little of the underlying principles upon which this danger was based. As early as the 16th century, some knowledge of the influence of altered intrathoracic pressures on cardiorespiratory function was gained from animal experimentation.

Fig. 2.—Andreas Vesalius (1514-1564), famous anatomist at the University of Padua, and one *of the first medical scientists.*

Andreas Vesalius,[2] a Belgian by birth and a noted anatomist and physician at the University of Padua, was one of the most outstanding figures in European medicine between Galen and Harvey (Fig. 2). Vesalius was an astute observer, an accurate recorder, and an inspiring teacher as indicated by his demonstration of altered respiratory function by animal experimentation, much as it is being done today, four centuries later. Allow me to refresh your memory on his erudite discussion with his students of the dangers of open pneumothorax during experiments on rabbits. After exposing the transparent parietal pleura through which the movements of the lung could be seen, he showed how the lung would fall away from the side of the chest wall on breaking the pleura and allowing the pleural cavity to communicate with the outside. If only one side of the chest was involved, the motion of the chest remained unchanged. However, if the opposite pleural cavity was opened, "the lungs are seen as the result of perforation to fall together and collapse.

The cardiac motion may not be observed for long, since suffocation of the animal will come on account of the collapse of the lungs. In order to restore the life of the animal, an opening is made in the upper part of the trachea, into which a pipe made from a reed is introduced. When it is breathed into, if the lung rises up, the animal receives air. The lung should be inflated to the degree to which it occupied the thorax in life. The heart now gathers strength and its motion will change beautifully. Therefore, by maintaining repeated inflation of the lung, you may have opportunity to examine the motion of the heart both by touch and sight as much as you desire." Thus, it is quite obvious that this great anatomist and scientist fully understood the ill effects of reduced pulmonary reserve. It is also obvious from his description of the experiment that a means of avoiding these untoward results, or of overcoming them once they were established, was possible through the use of positive pressure intratracheal insufflation. It seems incredible that the dangers associated with open pneumothorax continued to be remembered for four centuries, but that the principle involved in the method overcoming or obviating these hazards was forgotten, or at least was not associated with thoracic problems.

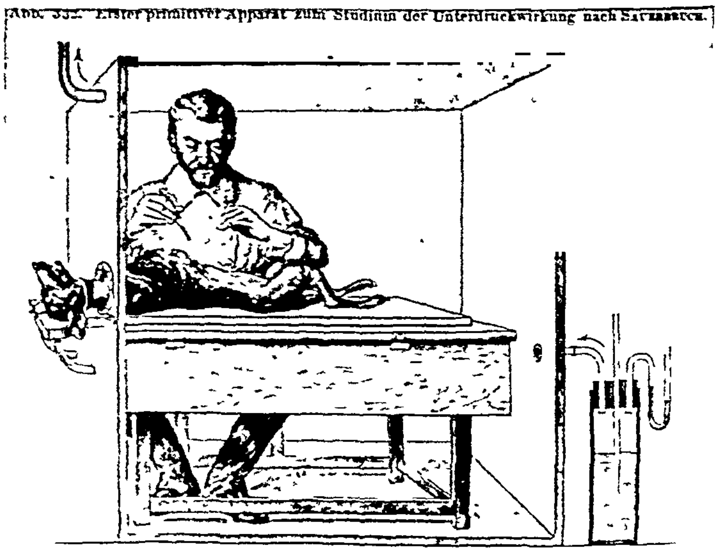


Abb. 33. Erster primitiver Apparat zum Studium der Unterdruckwirkung nach Sauerbruch.

Fig 3 —Negative pressure room developed by Sauerbruch for intrathoracic operations on animals A similar room was constructed for clinical use (after Sauerbruch)

Methods, procedures, and even principles seem to have a way of being rediscovered again and again, and so it was with this medical problem. Three centuries later, in 1903, Johann von Mikulicz, the noted German surgeon at Breslau, visited William Worrell Mayo at Rochester and discussed problems involved in surgery of the esophagus. Following this visit, he set his young assistant, Ferdinand Sauerbruch, at that time a young doctor of 27 years of age, to investigate methods of making intrathoracic surgery a safe procedure, with relatively little hope that a solution could be found. As a result of Sauerbruch's work, a negative pressure chamber was constructed in which open-chest operations could be safely performed under reduced atmospheric pressures[3, 4] (Fig. 3). When Brauer demonstrated that positive pressure insufflation of the lungs gave satisfactory results and was a far more practical arrangement, this type of anesthesia supplanted the negative pressure chamber. The work of Meltzer and Auer soon followed and, after overcoming certain inertia, led to the establishment of anesthetic methods and procedures in common use today.[5]

Although resection of an entire lung had been accomplished in animals as early as 1492 by Rolandus,[6] it did not become an established clinical procedure until in the early 30's when reports of a total pneumonectomy were made independently by Haight,[7] Nissen,[8] and Graham.[9] Two main factors repsonsible for the long delay in this field of surgery were (1) a lack of complete understanding of altered respiratory physiology during an open pneumothorax, and (2) the delayed development of anesthetic methods and techniques presently used in this field. Thus, in spite of observations made by Vesalius in the 16th century, almost four centuries elapsed before clinical use was made of this information.

With the operative risk associated with pulmonary resection reduced to an acceptable status, this field of surgery was extended to include resections of parts of both lungs usually performed for bilateral bronchiectasis. Eloesser[10] in 1933 was the first to report such a case, followed by Overholt[11] in 1937 with a report of a tri-lobectomy. In 1940, Graham[12] posed the question, "With how little lung tissue is life compatible?" At that time he reported the results of surgery in a patient in whom both lower and middle lobes were resected, the lingula on the left being considered as a left middle lobe, with only the two upper lobes remaining. Pulmonary resection was extended even farther in this patient, in whom, in addition to the four lower lobes, a portion of the right upper lobe was also excised for emphysematous blebs and bullae which had developed in association with bilateral bronchiectasis (Fig. 4). Reimann[13] and his co-workers have demonstrated on dogs that overdistention of the remaining lung tissue following massive reduction of lung capacity, such as by total pneumonectomy, is not accompanied by any significant increase in pulmonary resistance. Even with reduction of lung capacity to one upper lobe or 15 per cent of the normal, pulmonary artery pressures were no greater in the overdistended state than in the normally expanded state of the remaining lung tissue. These results corroborate those of Charbon and Adams[14] who found that filling of a pleural space with a plastic prosthesis following pneumonectomy did not improve the survival rate following further reduction of lung capacity to 15 per cent. Instead, he obtained no survivors at all in a group of 12 dogs, whereas, when no prosthesis was used, 4 of 13 dogs survived for weeks or months following operation. Graham's posed question was a very pertinent one and required further investigation in the laboratory. In experiments on dogs, reported by Phillips[15] and Rasmussen[16] and their associates, pulmonary capacity was reduced successfully to the right upper lobe or approximately 15 per cent of the original lung capacity. To accomplish this, it was necessary to reduce lung capacity in stages extended over a period of several weeks. This was accomplished by a combination of resection of the lower lobes as the first stage, and later occlusion of the bronchi to the remainder of the lung with the exception of an upper lobe, and subsequent

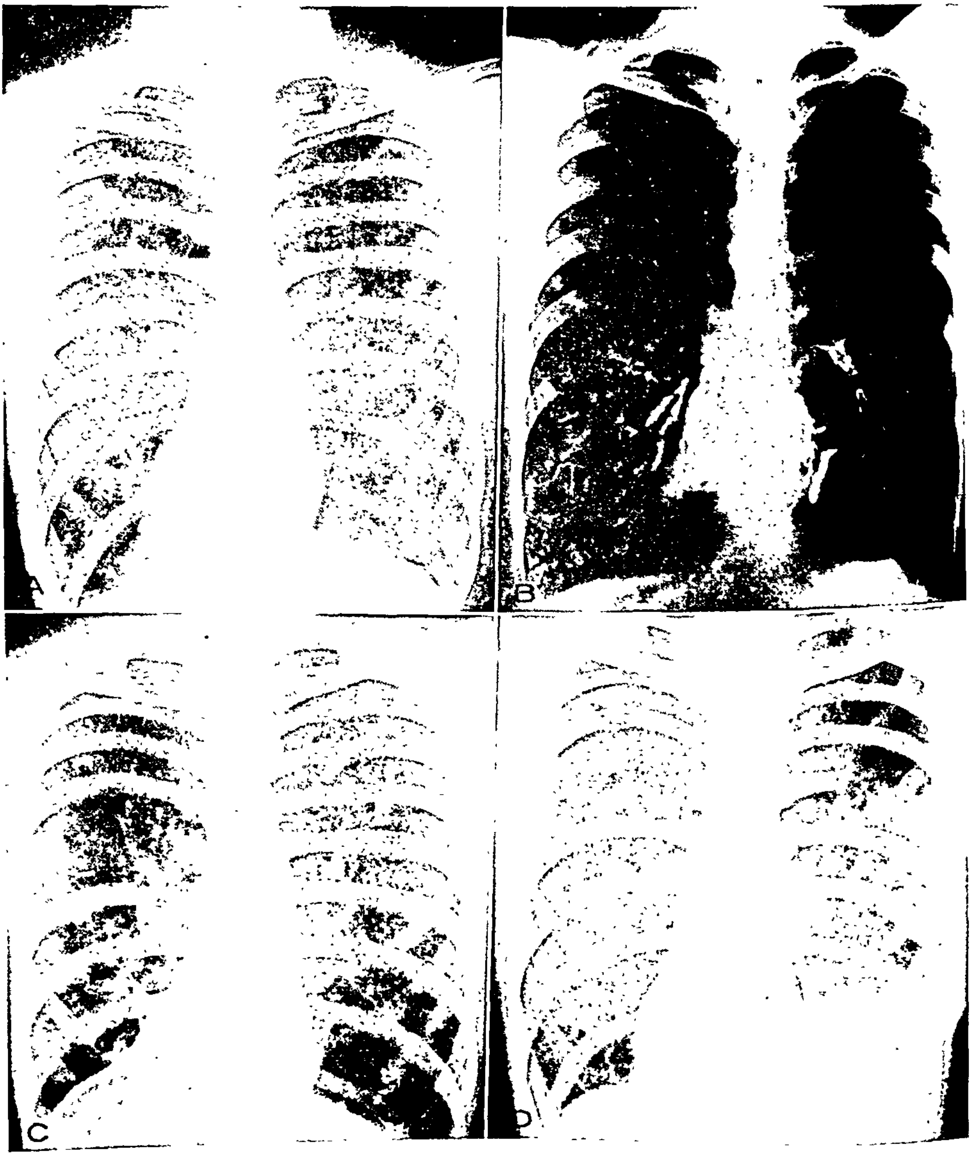


Fig. 4.—Roentgenograms of chest of a 33-year-old white man which show *(A)* normal posteroanterior view of chest exhibiting bilateral emphysema in the lower lung fields; *(B)* bronchogram showing bronchiectasis with complete collapse of both lower lobes and the right middle lobe, as well as involvement of the left upper lobe; and *(C)* and *(D)* x-ray appearance after resection of both lower lobes, the right middle lobe, as well as the lower portion of the right upper lobe for bullous emphysema, and resection of the lingula of the left upper lobe (patient's pulmonary reserve reduction was due to infection gradually over a period of years; compensation was adequate to obviate serious cardiopulmonary symptoms following bilateral resection).

collapse of those lobes by absorption of the entrapped air. Carlson and his co-workers,[17] at a later date, were able to accomplish this marked reduction in capacity to 15 per cent by a staged resection of the remaining portion of the lung. However, only 4 of 13 animals survived this method; the remainder died of excessive (right) heart strain (pulmonary artery pressures were increased by 100+ per cent). Thus, the dog's ability to tolerate marked reduction of lung capacity was governed, at least in part, by the rate at which the diminution was made. Furthermore, when a small physiologic shunt remained, such as that represented by the remaining atelectatic lobes, the risk of reducing the capacity to this small amount was lessened (Fig. 5, *A*).

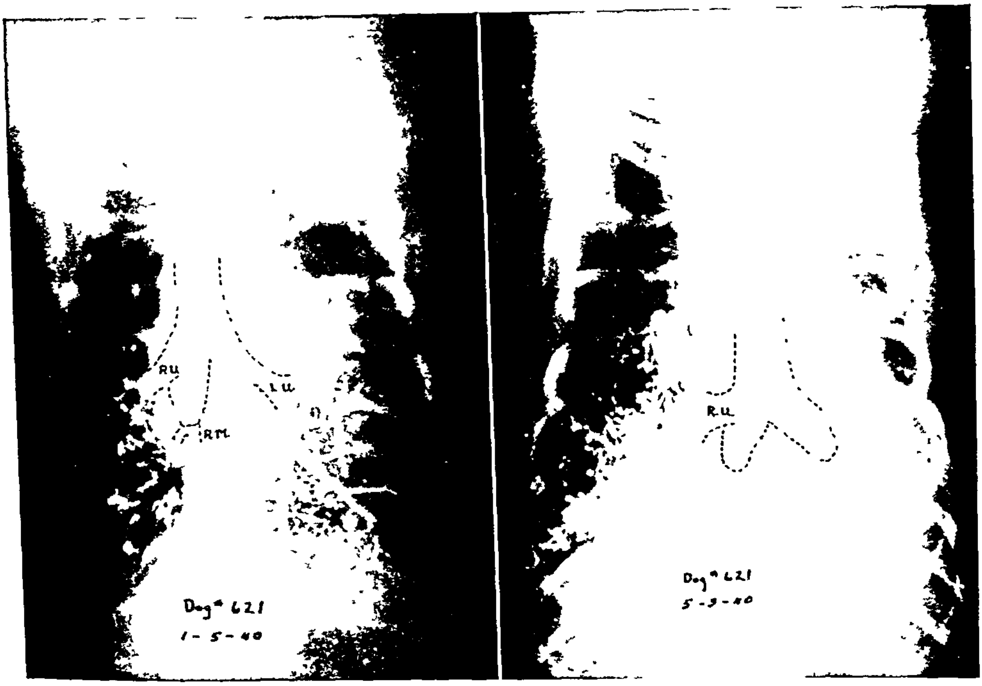


Fig 5*A*—Two bronchograms of a dog made after a staged reduction in lung capacity by a combination of surgery and bronchial stenosis On the left, the capacity has been reduced to both upper lobes and the right middle lobe or approximately 38 7 per cent of normal through bilateral excision of both lower and the right accessory lobes On the right, the capacity has been further reduced to only the right upper lung lobe or approximately 15 per cent of normal through bronchial stenosis of the right middle and the left upper lobes By staging the reduction of lung capacity slowly, this animal was able to tolerate reduction to only this small per cent (From Rasmussen et al[16])

Following this marked reduction in capacity, these animals appeared to be healthy, remained well nourished, and were able to tolerate moderate exercise. They were usually active in the kennel and, although somewhat dyspneic on exercise, did not show evidence of cyanosis. Upon sacrificing such an animal having only 15 per cent of his original lung capacity, the remaining lobe was found greatly overdistended and, on microscopic examination, revealed some fragmentation of the peripheral respiratory units (Fig. 5, *B*). This, however, did not represent a true emphysema since no increase in fibrous tissue in the alveolar walls was observed. In spite of this marked alteration of microscopic appearance, these animals tolerated a rarefied atmosphere remarkably well. A test of their tolerance to such a situation was made by placing them in an evacuation chamber and reducing the pressure therein until consciousness was lost. When normal dogs were subjected to this procedure they were able to tolerate a reduction in pressure to approximately 221.6 mm. Hg (comparable to an altitude of 30,400 feet and 6.25 per cent O_2), or a pressure similar to that tolerated by man before losing consciousness. Dogs with only three functioning lung lobes, or approximately 38 per cent of normal, had the same tolerance. When the one-lobe dogs (15 per cent of normal) were subjected to this test, consciousness was lost at 270 mm. Hg (altitude of 25,833 feet and only 7.75 per cent O_2), thus demonstrating a remarkable ability to oxygenate the blood with but a small amount of functioning lung tissue (Table I). Although these animals appeared well for a few weeks or months following these experiments, most of them died much earlier than would have been otherwise expected. At the time these experiments were made, the mechanism of death was not well understood.

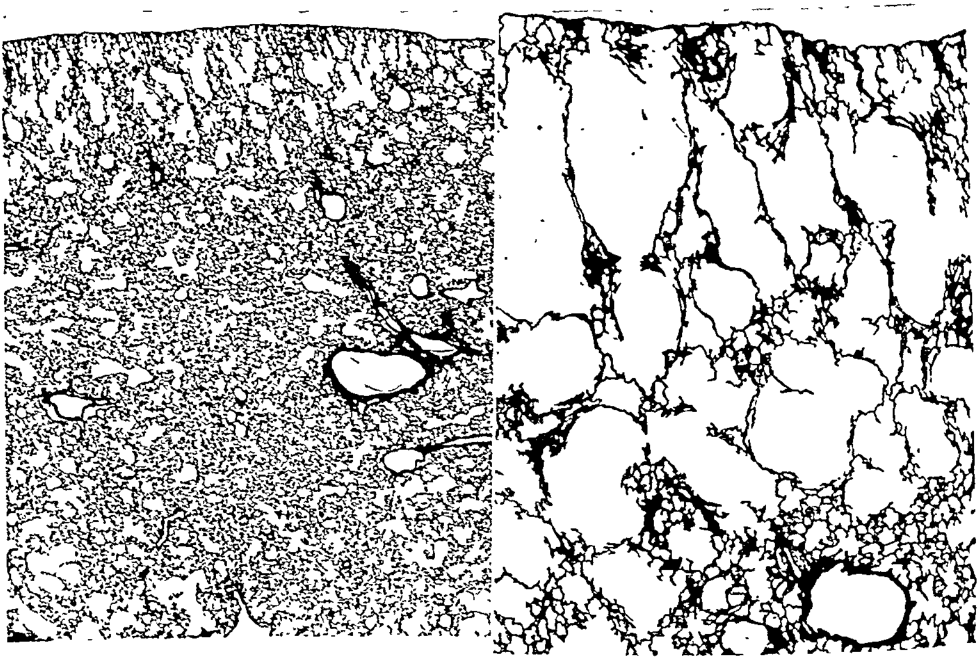


Fig. 5*B*.—Microscopic appearance of a dog's lung following reduction in pulmonary capacity to one upper lobe or 15 per cent of normal. Note marked tendency to overdistention of terminal respiratory units, especially at the peripheral portion of the lung, with marked dilatation of terminal respiratory units. Definite compensatory emphysematous changes are seen in the alveolar ducts and sacs; however, *no increased fibrous tissue production* is present. (*Left*, ×7—*Right*, ×20; both reduced $\frac{3}{7}$.) (From Rasmussen.[16])

The ability of human beings to tolerate marked reduction in pulmonary capacity has been repeatedly demonstrated by the use of bilateral pneumothorax in the treatment of pulmonary tuberculosis. Here again it was necessary gradually to produce collapse in order to avoid cardiopulmonary distress. An example of this marked reduction in capacity tolerance is illustrated by a

TABLE I. RESPIRATORY RESERVE AT REST AS DETERMINED BY REDUCTION OF ATMOSPHERIC PRESSURE

STANDARD ATMOSPHERIC PRESSURE	
ALTITUDE FEET	PRESSURE MM. Hg
0	760
1,000	733
5,000	632.4
10,000	522.6
15,000	428.8
20,000	349.2
25,000	282
30,000	225.6
35,000	178.7
40,000	140.7

CONDITION OF ANIMAL AND % OF FUNCTIONING LUNG	NO. OF DOG	ALTITUDE TOLERATED	TIME OF ASCENT MINUTES	AVERAGES	
				ALTITUDE FEET	PRESSURE MM. Hg
Normal (6 lobes) 100%	1	30,500	10	30,400	221.6
	2	30,500	10		
	3	29,500	10		
	4	32,000	8		
	4	29,500	11		
3 lobes 38%	917	32,000	6	30,000	225.6
	993	32,000	7		
	3	25,000	7		
	637	31,000	9		
	871	30,000	9		
2 lobes 23%	636	27,500	4	26,000	269.8
	869	24,500	6		
1 lobe 15%	635	26,500*	5	25,833	272
	621	25,000†	6		
	695	26,000	10		

Table shows respiratory reserve at rest during the lowering of pressure in an evacuation chamber in dogs with normal lung capacity as well as with reduced lung capacity to 38, 23, and 15 per cent of normal. Note marked degree of tolerance to rarefied atmosphere with lower oxygen available to animals with only 15 per cent of original capacity. The percentage of oxygen available at 30,000 feet altitude or 230 mm. Hg pressure is approximately 6.4 per cent, whereas that available at 26,000 feet altitude or a pressure of 270 mm. Hg is approximately 7.7 per cent. (From Rasmussen et al.[16])

*Failed to recover.

†Did not become unconscious.

patient treated by Dr. Victor S. Randolph. A roentgenogram of this patient taken at the end of deep expiration showed scarcely any inflated lung tissue. The second view taken at the end of deep inspiration revealed relatively little functioning lung on either side (Fig. 6). During this phase of the patient's treatment, he was at bed rest and therefore the requirements for oxygen were considerably reduced. (This was a young adult male patient and therefore the lung tissue might be expected to tolerate a greater degree of collapse than in an older individual.)

From the evidence these patients revealed and the results of animal experimentation, it appeared that total pneumonectomy was a procedure that should be well tolerated with little risk to the patient. In normal, healthy animals, this has been proved beyond a doubt. Likewise, in the younger individuals, cardiopulmonary function has been repeatedly demonstrated to be quite adequate, not only while at rest, but also sufficient to insure a relatively normal way of life.

However, as more experience in this problem was obtained, the mortality rate of this operation in older people (above 60 years of age) was found to be definitely increased. Furthermore, the cause of death in some patients was inadequately explained by the results of pulmonary function studies prior to surgery. This led to further investigation of the problem on dogs, in which pulmonary resistance and pulmonary flow rates were correlated with pulmonary function values before and after varying degrees of reduction in lung capacity.[18]

It was fully appreciated that in animals only relatively normal lung tissue was involved, whereas in clinical cases, dealing with inflammatory, neoplastic, or degenerative disease, a combination of changes in lung tissue structure, as well as function, might very well play an important role. These experiments revealed that when a dog's lung capacity was rapidly reduced to 15 or 20 per cent of normal, pulmonary vascular resistance was more than doubled, and that an intolerable level of pulmonary hypertension occurred in a high percentage of animals. Furthermore, it was found that a demand for increased cardiac output during exercise further increased the degree of cardiac strain.

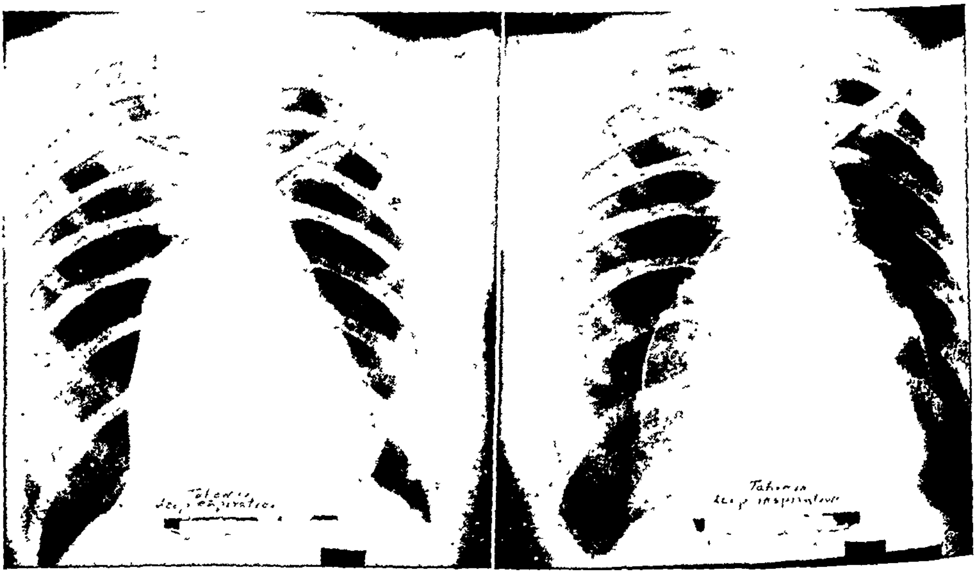


Fig. 6.—Two roentgenograms of the chest of a young, white man taken during deep expiration on left and on deep inspiration on right. This patient was being treated for bilateral pulmonary tuberculosis by bilateral pneumothorax. Note marked degree of collapse of both lungs by therapy. Since the requirements for oxygen at rest were quite low and since this was a relatively young individual, this marked degree of reduction in lung capacity was tolerated.

On the other hand, blood oxygen saturation suffered relatively little (5 per cent) while the animal was at rest, even with reduction of lung capacity from 50 to 15 per cent. During exercise, the saturation level dropped precipitously but could be restored to normal immediately by the administration of oxygen (Fig. 7).

In patients with bilateral alteration of the lung which is due to inflammatory, degenerative or other conditions, the pulmonary vascular resistance may be increased by as much as 100 per cent. This is especially true in the so-called older age group. Thus, removal of an entire lung may carry considerable risk. In nonmalignant disease it is frequently possible to limit pulmonary resection, thus preserving maximum lung capacity. However, in the case of malignant lesions, it has been generally believed that removal of the entire lung along with adjacent tumor-bearing tissue is the operation of choice, when it can be tolerated by the patient. In patients of this older age group with an already reduced pulmonary reserve, a sudden additional reduction in lung capacity by pneumonectomy may lead to an intolerable degree of increased cardiac strain due to increased pulmonary vascular resistance without lowering blood oxygenation to a dangerous level. Postoperative alteration in pulmonary tissue and chest wall function may well augment the serious degree of increased pulmonary vascular resistance produced by pulmonary resection. Since the risk of pneumonectomy is increased in the older age group having poor pulmonary reserve, repeated attempts have been made to determine the "resection tolerance" of such patients prior to surgery. Studies made by a number of investigators[19] have increased our knowledge of factors concerned with this problem. In the past several years, special attention has been given to the problem of changes in pulmonary vascular resistance attending the resection of lung tissue both in animals and in man.[20]

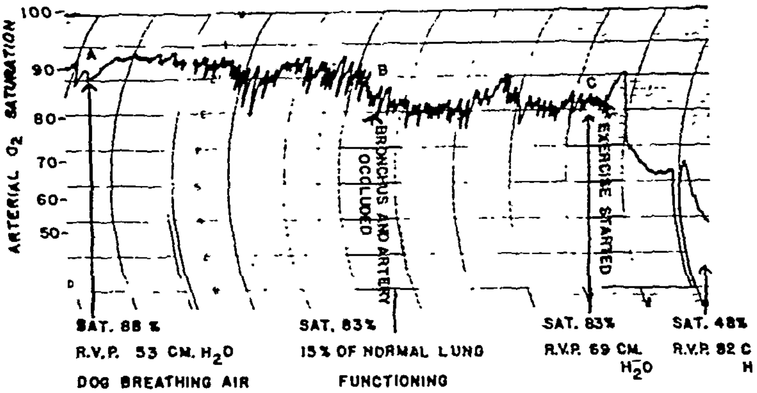


Fig. 7.—Dog 737—March 25, 1952. Continuous recording oximeter tracing of oxygen saturation in the dog during reduction in pulmonary capacity from 50 per cent on the left to 15 per cent by suddenly obstructing the bronchus and vessels to all except one upper lobe at point *B*. *Saturation levels, right ventricular pressures* and other data are indicated below the tracing. The record reveals a marked elevation in right ventricular pressure from 53 to 69 *cm.* of water with reduction in lung capacity from 50 per cent at *A* to 15 per cent at *B* and *C*. Oxygen saturation during this period was reduced by only 5 per cent. The effect of exercise begun at *C* on oxygen saturation as well as right ventricular pressure is demonstrated. When oxygen was given by nasal catheter, the saturation level became suddenly elevated to *normal*; however, right ventricular pressures remained high. (From Adams et al.[15])

In young, healthy people, both pulmonary function studies as well as pulmonary vascular data show a considerable range of safety in the majority of cases following total pneumonectomy. Blood oxygen saturation is usually normal during the resting state and shows only mild elevation during exercise. The cardiac output is likewise normal at rest, and increases in a normal manner with exercise. The following patients will serve as examples of fairly characteristic responses following pneumonectomy in older people. The fatalities which occurred in Cases 1 and 2 were due to intolerable pulmonary hypertension and cardiac failure, occurring 19 and 11 days, respectively, following pneumonectomy for malignant disease.

CASE 1.—The first patient (O. C., Case 1) was a 66-year-old white man whose pulmonary function studies made before operation showed a moderate reduction of ventilatory capacity. At the time of surgery, preocclusion pressure of the pumonary artery showed a mean of 39 cm. of water. This pressure rose to 53 cm. of water after occlusion of this artery. The surgical procedure was tolerated quite well and his immediate postoperative course was quite satisfactory. Oximetric studies revealed decreased saturation of blood oxygen; however, this was easily corrected with a very low flow of oxygen via oropharyngeal catheter. Although the patient was digitalized, his condition did not improve and he died on the nineteenth postoperative day of cardiorespiratory failure (Fig. 8).

Case 2.—The second patient (R. R., Case 2) was a 59-year-old white man who underwent a total pneumonectomy for primary carcinoma of the left lung involving the left chest wall. The general physical examination of this patient showed him to be in relatively good condition prior to surgery. Likewise, pulmonary function studies revealed only mild to moderate reduction in functional values. During operation, preocclusion pressures were 48/12 mm. Hg. Following occlusion, the pressures rose to 60/12 mm. Hg. Because of this high pulmonary resistance, he was started on prophylactic digitalis. He appeared to be progressing satisfactorily, although the electrocardiogram revealed some premature auricular beats. His convalescence on the fifth postoperative day was quite satisfactory, the blood oxygen saturation being 93 per cent on air with an elevation to 98 per cent on oxygen. X-ray studies showed a satisfactory postoperative appearance of the chest. By the ninth postoperative day, he became rather lethargic and again showed evidence of auricular fibrillation. The oxygen saturation studies still remained good, being 95 per cent on air and 100 per cent on oxygen on the tenth day. On the following day, he suddenly became quite dyspneic and died (Fig. 9).

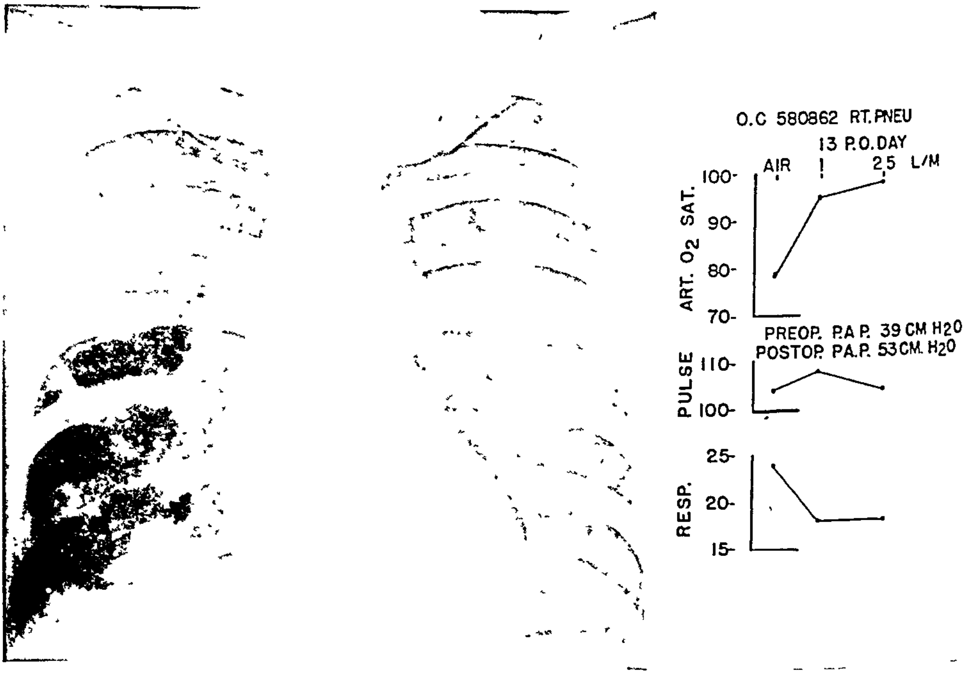


Fig. 8.—Case 1 (O. C.). Roentgenogram of the chest which reveals a bronchogenic carcinoma of the right lung. Data on *right* were obtained 13 days following surgery, except for preocclusion and postocclusion pressures of pulmonary artery at the time of surgery. Note lower oxygen saturation to 80 per cent which was elevated to a satisfactory level with only 1 L. per minute of oxygen flow via an oropharyngeal catheter. Death occurred on the ninteenth day after operation of cardiac failure.

Case 3.—This next case is presented to indicate how data from pulmonary function studies appeared unsatisfactory, whereas those obtained from investigation of pulmonary circulation proved to be quite adequate, and where the results of surgery were satisfactory. This patient was a 63-year-old white man (H. M., Case 3) who had had a pneumonectomy for a primary carcinoma of the left lung. Pulmonary function studies showed relatively normal ventilatory values, but an increased residual volume and a markedly decreased maximum mid-expiratory flow, and timed vital capacity was definitely below normal. Circulatory studies on this patient showed a normal pulmonary artery pressure both at rest and during exercise before operation. Likewise, arterial oxygen saturation was within satisfactory limits. Pulmonary vascular resistance decreased during exercise while cardiac output increased. This patient underwent a left pneumonectomy without difficulty. The mean pulmonary artery pressures have remained about the same during the 4-month period of study since operation. The pulmonary vascular resistance has continued low and has permitted an adequate increase in cardiac output without the necessity of increased pulmonary artery tension.

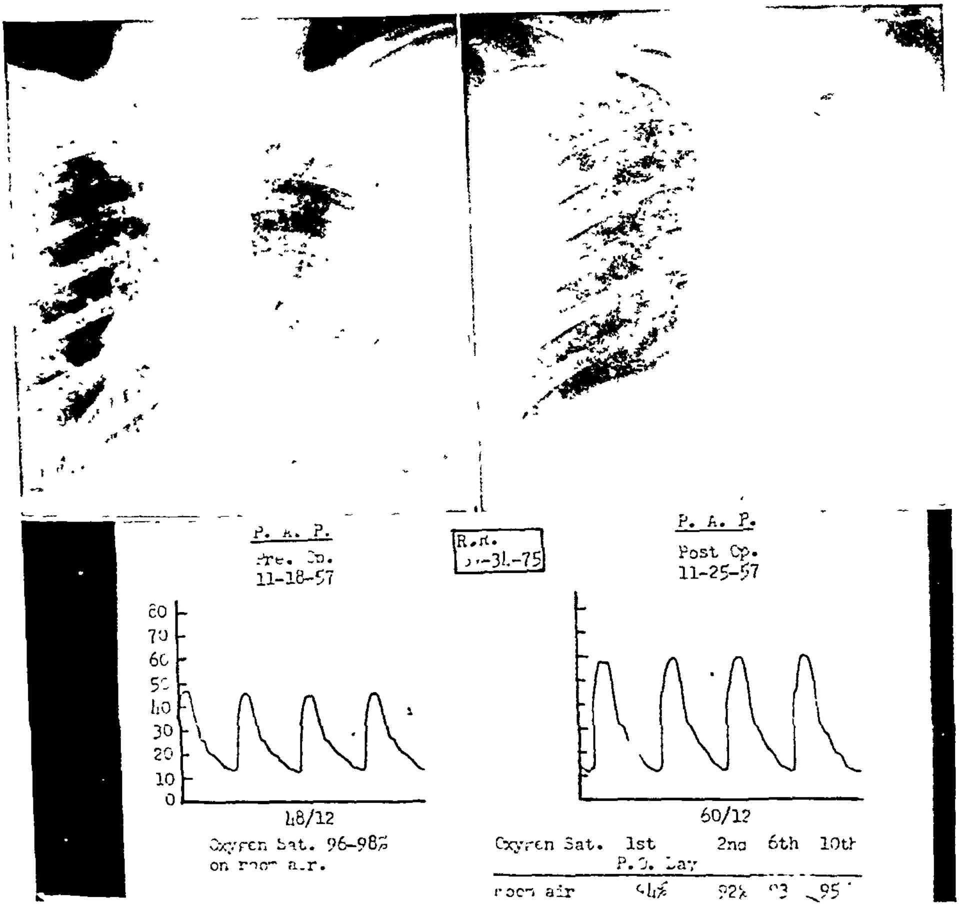


Fig. 9.—Case 2 (R. R.). Roentgenograms of the chest made before and following a left pneumonectomy. Preocclusion pressures were 48/12 and postocclusion 60/12 mm. Hg. Oxygen saturation levels were quite satisfactory both before and following surgery. The patient died on the eleventh day after operation of cardiac failure.

Case 4.—This next patient demonstrated opposite results during study before operation, that is, the results of pulmonary function studies were excellent in all respects and tended to indicate that the operation would carry little risk. He was a 61-year-old white man (J. D., Case 4) in whom a pneumonectomy for primary carcinoma of the right lung was done. At surgery, the preocclusion pressure in the pulmonary artery was found to be double the normal value. After occluding the artery to the side to be removed, this pressure increased 10 to 15 per cent. Because of the location of the tumor, it was necessary to do a total pneumonectomy. In view of this patient's marked pulmonary resistance and pulmonary hypertension, all precautions were taken to bring him through the postoperative period. This included a tracheostomy, oxygen therapy, absolute bed rest, and digitalization of the heart. He responded in a satisfactory manner and was kept on this routine for 4 weeks. At this time, a study of his lesser circulatory values revealed approximately the same findings as at the time of operation. Mild exercise increased these pressures materially. Repeated tests made at 2 and 4 months after surgery showed a gradually decreasing level of pulmonary artery pressures with relatively normal blood oxygen saturation. However, as the pulmonary artery pressures were reduced in amount, the cardiac output was likewise reduced, indicating a remaining high pulmonary resistance. This patient was allowed to go home 6 weeks after operation and was readmitted for these studies. Shortly after returning home on the last occasion, he suddenly died. He had been receiving x-ray therapy for metastases and it was felt that spread of the tumor may have played a role in the gradually diminishing cardiac function.

CHRONIC PULMONARY HYPERTENSION

After patients have survived the ablation of an entire lung, the question might be raised, "How well will this reduced pulmonary capacity be tolerated during later life?" Should the patient change his occupation if it requires strenuous exercise or work and lead a more sedentary type of life? What may be anticipated in the way of life expectancy? It is well known that some patients may continue their normal occupation for many years without difficulty. On the other hand, either shortly after operation or at some period of years later, so-called "pulmonary cripples" have developed with complete incapacitation and reduction of the normal life span.

In order to answer some of these questions, a study was begun some 10 years ago and accelerated during the past 3 years with financial aid from the American Cancer Society. This has enabled the collection of considerable data on 55 patients whose operation had been performed up to 16 years before the study. These patients were admitted to the hospital for a period of 2 or 3 days during which time a detailed investigation included (1) securing data for clincial evaluation, (2) measurements of various aspects of pulmonary function, and (3) obtaining pressure flow values of the lesser circulation. A correlation of the results from each evaluation was made. These detailed studies extended from a few weeks to several years following surgery, in addition to studies made prior to operation and at the time of operation. The results of this study to date would indicate that in general the younger age group of patients, namely, under 50 years of age, revealed little or no difficulty in either pulmonary or vascular reserve during the several years after operation. Functional studies showed some decrease in ventilatory capacity; however, diffusion ability remained normal and adequate, permitting reasonable degrees of exercise or work. Likewise, pulmonary-circulatory studies showed normal resting pressure flow values with only moderate elevation of pressure on exercise (Fig. 10—J. K., Case 5). Some of these patients have been followed over a period of 4 or 5 years, and the pulmonary and circulatory determinations have remained approximately constant. On the other hand, some patients under the age of 50 remained healthy and active for a period of 5 to 10 years at which time they began to develop symptoms of cardiopulmonary insufficiency when active, and subsequently became decompensated, as indicated by the following example.

CASE 6.—This patient was a 56-year-old white man (O. L., Case 6), who, 11 years previously at the age of 45, had had a right pneumonectomy for bronchogenic carcinoma of the lung. After operation, he had an uneventful convalescence and was followed in the Out-patient Department. Eight years following pneumonectomy he began showing signs of increasing pulmonary insufficiency with marked dyspnea, orthopnea, and chronic nonproductive cough. On the early morning of admission, he awakened and coughed up two or three tablespoons of bright red blood. General physical examination showed nothing remarkably abnormal. However, cardiopulmonary function evaluation revealed lowered ventilatory values, blood-oxygen saturation of 90 per cent, and a right ventricular pressure of 56/0 mm. Hg. A moderate degree of exercise for one minute lowered the saturation to 86 per cent and elevated the right ventricular pressure to 85/0 mm. Hg. This patient's condition has continued to worsen and he is at the present time a pulmonary cripple, being unable to tolerate more than walking across the room.

FUNCTIONAL CLASS I.

T.L.C.	3.85 L.	
V.C.	2.05 L. (68%)	
R.V.	1.5 L.	
M.B.C.	57.0 L./min. (60%)	
1 sec V.C.	74%	

	Rest	Exer.
Pulm. Art. Press.	$\frac{25}{8}$ (14)	$\frac{41}{17}$ (25)
Art. O_2 Sat.	95%	97%
Pulse Rate	110.0	146.0
O_2 Consumption	235.0	579.0
Cardiac Output (L./min.)	5.5	9.3

FIG. 10.—Case 5 (J. K.) Roentgenogram of chest and data collected from cardiopulmonary evaluation on a 37-year-old white woman 3 years after a left pneumonectomy. Note relatively good pulmonary function values, satisfactory arterial oxygen saturation levels at rest and during exercise, normal cardiac output response to exercise with only moderate increase in pulmonary artery pressure as compared to that of the resting state which is at a normal level.

T.C.L. = total lung capacity; *V.C.* = vital capacity—per cent of normal predicted for subject with two lungs; *R.V.* = residual volume; *M.B.C.* = maximum breathing capacity—per cent of predicted value for a normal chest with both lungs; 1 sec. V.C. = per cent of the vital capacity expired in the first second; *Pulm. Art. Press.* = pulmonary artery pressures (mm. Hg) (mean pulmonary artery pressure in parentheses); *Art O_2 Sat.* = arterial oxygen saturation; *O_2 Consumption* = oxygen consumption (ml./min.). (From Harrison et al.[20])

In still other patients, cardiopulmonary insufficiency appeared and was markedly accentuated during mild upper respiratory infections. The following case illustrates this point.

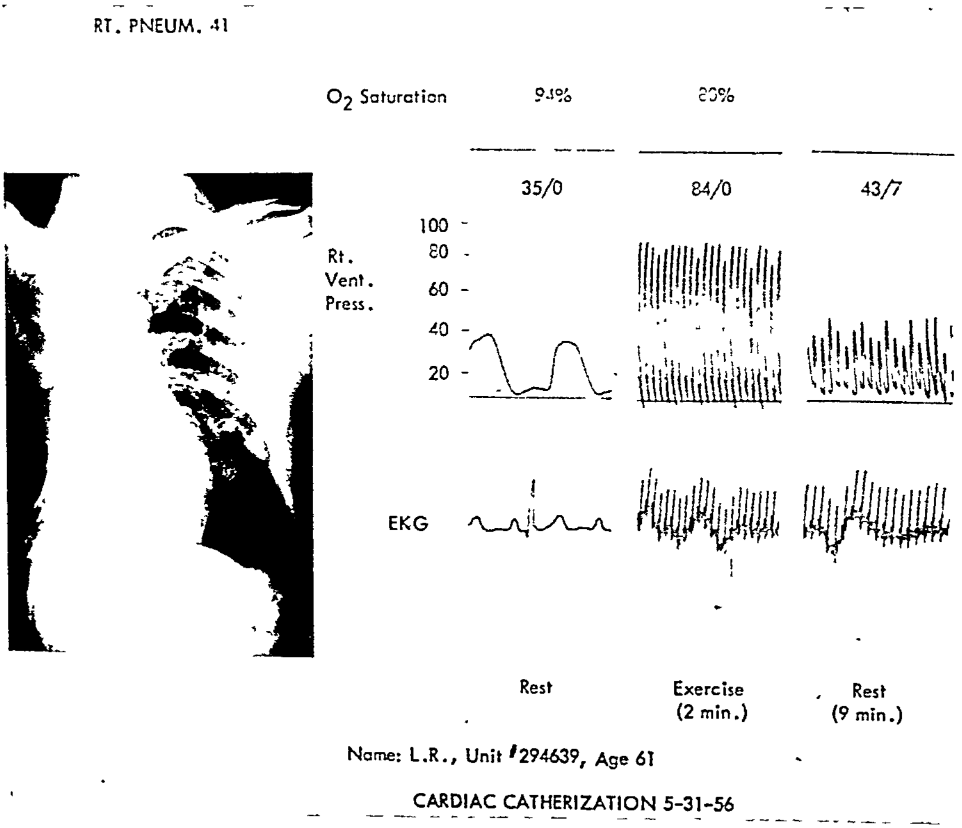
CASE 7.—This patient was a 61-year-old white man (L. R., Case 7) who had had a right pneumonectomy for bronchogenic carcinoma 13½ years previously at the age of 47.

Two years later, an empyema developed in the right chest for which a Schede thoracoplasty was made. For 10 years following pneumonectomy he was able to do full-time office work without any evidence of a cardiopulmonary problem. At the end of that time, there developed one-flight exertional dyspnea and a mild nonproductive cough. Physical examination showed signs of mild decompensation. He had had a mild upper respiratory infection prior to admission which had accentuated his dyspnea. Pulmonary function studies showed relatively normal values, except for a low maximum breathing capacity. His oxygen saturation at rest was 94 per cent. Cardiac catheterization showed a pressure of 35/0 mm. Hg. With only moderate exercise, his pressures elevated to 84/0 mm. Hg and the saturation was lowered to 80 per cent of normal. With the subsidence of his upper respiratory infection, his symptoms became much relieved and he continued his routine work. When the cardiopulmonary studies were repeated 2 years later, 15½ years following pneumonectomy, the pulmonary function values were somewhat diminished and arterial oxygen saturation was 94 per cent. Pulmonary artery pressure at this time was only mildly elevated but became almost doubled in amount on moderate exercise. The oxygen saturation, however, was not lowered by exercise. This patient has subsequently become gradually less able to carry on his work without difficulty. Although not a pulmonary cripple at the present time, he has had to reduce his activities and lead a very sedentary type of life (Fig. 11, *A* and *B*).

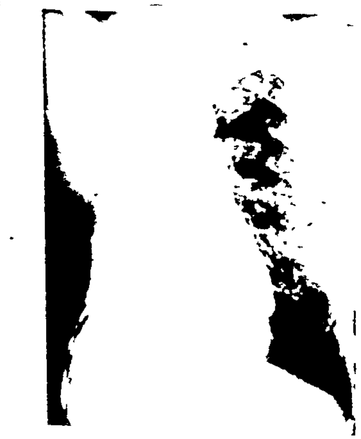
In older patients who underwent surgery after the age of 60, acute or chronic pulmonary hypertension was more likely to develop than in patients under 50 years of age. Although our clinical data are as yet insufficient percentagewise for prognostication, patients over 60 years of age are more likely to develop pulmonary hypertension sooner than are those patients whose surgery was performed before 50 years of age. This would suggest that if surgery is performed in the younger age group, a degree of compensation may occur over a period of years following surgery which will offset the development of chronic pulmonary hypertension. The following case is an illustration of this point.

CASE 8.—This patient was a white man, 66 years of age at the time of pneumonectomy (J. S., Case 8), whose convalescence after operation was quite satisfactory. Within 5 years following operation, he began showing an increasing amount of dyspnea on mild exertion. Eight years later, he was having much more difficulty and was admitted for study. Pulmonary function data indicated a moderate to severe degree of reduction in maximum breathing capacity and timed vital capacity. In spite of this, the oxygen saturation was 96 per cent. Pulmonary artery pressures at rest were markedly elevated to 75/35 with a mean of 48 mm. Hg. On moderate exercise, this rose to 112/45 with a mean of 67, at which time the oxygen saturation had dropped to 90 per cent. He was put on digitalis and reduced activity with considerable relief of symptoms. However, in spite of this regimen, his degree of incapacitation continued to increase. He died suddenly of cardiac decompensations, having been a pulmonary cripple during the preceding 4 or 5 years (Fig. 12).

This study has led us to believe that a number of things may be considered when accurate determinations of the pulmonary and circulatory status are made prior to, or at the time of, surgery for pulmonary abnormalities. In the case of nonmalignant pulmonary lesions, added precautions may be taken to insure adequate cardiopulmonary reserve following surgery. In some conditions, a preoperative period of medical management may alter the pulmonary lesion to such an extent that cardiopulmonary reserve may be enhanced and



A.



FUNCTIONAL CLASS III.

T.L.C.	2.8 L.
V.C.	1.2 L. (34%)
R.V.	1.6 L.
M.B.C.	31.0 L./min.(34%)
1 sec V.C.	71%

	Rest	Exer.
Pulm. Art. Press.	$\frac{38}{13}$(21)	$\frac{56}{30}$(39)
Art. O_2 Sat.	94%	95%
Pulse Rate	88.0	116.0
O_2 Consumption	206.0	591.0
Cardiac Output (L./min.)	3.2	6.3

B.

FIG. 11.—Case 7 (L. R.). *A*, Roentgenogram of chest and data obtained on cardiopulmonary evaluation 13½ years after a right pneumonectomy; *B*, the same information obtained 2 years later, namely, 15½ years postpneumonectomy. The data obtained in *A* were shortly after an upper respiratory infection which had led to some degree of cardiac decompensation. Note a lowering of pulmonary function values as well as an increased amount of lesser circulatory pressure at the time of this patient's infection as compared to that obtained after the infection had subsided. (Same key as in Fig. 10.) (*B*, From Harrison et al.[29])

surgery made less hazardous. In a case of neoplastic disease in which the lesion is peripherally located and reserve appears to be limited, removal of less than an entire lung may well be adequate for ablation of all tumor-bearing tissue. Although total pneumonectomy may be the procedure of choice in most of these patients, many long-term survivals have been reported following ablation of one or two lung lobes. When it is essential to remove an entire lung in patients with low cardiopulmonary reserve, the employment of various measures for supporting the individual through surgery may insure a more satisfactory result. Since increased pulmonary resistance requires a greater right heart load with increased pulmonary pressures for the maintenance of adequate cardiac output, reduction of activity through sedentary types of employment, restriction of other physical activities, and the prevention of pulmonary infections may go far in preventing the development of a "pulmonary cripple."

FUNCTIONAL CLASS IV.

T.L.C.	5.66 L.	
V.C.	2.5 L. (75%)	
R.V.	3.03 L.	
M.B.C.	32.0 L./min.(43%)	
1 sec V.C.	46%	
	Rest	Exer.
Pulm.Art.Press.	$\frac{75}{35}$(48)	$\frac{112}{45}$(67)
Art. O_2 Sat.	96%	90%
Pulse Rate	84.0	92.0

Fig. 12.—Case 8 (J. S.). Roentgenogram of chest and data collected at cardiopulmonary evaluation on a 74-year-old white man 7½ years after a left pneumonectomy. Note some lowering of pulmonary function values with, however, a normal arterial oxygen saturation during rest. The pulmonary artery pressures in this patient were extremely high and became markedly elevated with moderate exercise. (Same key as in Fig. 10.) (From Harrison et al.[20])

The modern trend in pulmonary surgery is to conserve on the amount of lung resected. Furthermore, attempts are made to re-establish functioning lung tissue when it has been disabled by disease or trauma. An example of this is seen in the use of bronchoplasty following bronchial stenosis due to pulmonary tuberculosis. Another example is the re-aeration of an atelectatic lung following traumatic stenosis of a primary bronchus. The report given this morning by Dr. Long and his co-workers was another step forward in this direction. Progress has been made in this field by several workers[21-24] who have reported a number of instances of successful re-aeration of an atelectatic lung. Studies have at times not been available by which to determine the physiologic status of these re-aerated lungs. It is hoped that in the future, surgeons who have this opportunity may make physiologic studies which will determine if the human lung reacts in a manner similar to that of the dog's lung in a state of chronic atelectasis. Although the studies reported by Dr. Long show that a re-inflated atelectatic lung in dogs has only 25 to 30 per cent of its original functional value, nonetheless this small amount of function may mean considerable to the individual as cardiopulmonary reserve diminishes during later years. Furthermore, the functioning lung tissue would then be distributed to both sides of the tracheobronchial tree.

Time has not permitted giving credit to the many workers who have made valuable contributions in this field. This will appear in the published article. In addition, I wish to give a full measure of credit to Drs. Harrison, Long, Reimann, Benfield, Nigro, Attalla, Borquez Vial, Mikouchi, and Shankarappa, who have contributed materially in the investigative work referred to in this discussion. With the continuing increase in life expectancy, this problem in connection with lung surgery assumes an increasing importance. Much more work needs to be done and a step in this direction is replacement of a diseased lung by transplantation of a healthy one. Transplantation of liver, spleen, kidney, lung[25] and other organs has proved to be technically assured. Inroads on the problem of the tissue "rejection phenomenon" are gradually being made. With continued united effort, scientific endeavor, and imagination, what is mpossible today may be an accepted procedure in the not-too-distant future.

REFERENCES

1. Castellanos, M., Thompson, R. G., Adams, W. E., Perkins, J. F., Jr., and Webber, W.: Use of the Recording Oximeter in Management of Postoperative Oxygen Therapy, J. THORACIC SURG. 29: 419, 1955.
2. Vesalius, Andreas: Cited by Homans, J.: A Textbook of Surgery, Springfield, 1931, Charles C Thomas, publisher, p. 760.
3. Killian, Prof. Hans: Scope and Utility of Differential Pressure in Thoracic Surgery, Anesth. & Analg. 17: 154, 1938.
4. Sauerbruch, F.: Present Status of Surgery of the Thorax, J. A. M. A. 51: 808, 1908.
5. Meltzer, S. J., and Auer, J.: Continuous Respiration Without Respiratory Movements, J. Exper. Med. 11: 622, 1909.
6. Rolandus: Quoted by Murphy, J. B.: Surgery of the Lung, J. A. M. A. 31: 341, 1898.
7. Haight, C.: Total Removal of Left Lung for Bronchiectasis, Surg. Gynec. & Obst. 58: 768, 1934.
8. Nissen, Zentralbl. f. Chir. 47: 1003, 1931.
9. Graham, E. A., and Singer, J. J.: Successful Removal of an Entire Lung for Carcinoma of Bronchus, J. A. M. A. 101: 1371, 1933.
10. Eloesser, L.: Bilateral Lobectomy, Surg. Gynec. & Obst. 57: 247, 1933.
11. Overholt, R.: Trilobectomy, J. A. M. A. 109: 127, 1937.
12. Graham, E. A.: With How Little Lung Tissue Is Life Compatible? Surgery 8: 239, 1940.
13. Reimann, A. F., Long, E. T., Adams, W. E., Ozoa, A. K., and Nigro, S. L.: Pulmonary Artery Studies. Does Overdistention of the Lung Cause Hypertension? Dis. Chest. (In press.)
14. Charbon, B. C., and Adams, W. E.: A Study to Determine the Effect of Prevention of Overdistention of the Remaining Lung Tissue on the Elevated Right Ventricular Pressures Following the Resection of Lung Tissue in Dogs, J. THORACIC SURG. 23: 341, 1952.
15. Phillips, F. J., Adams, W. E., and Hrdina, L. S.: Physiologic Adjustment in Sublethal Reduction of Lung Capacity in Dogs, Surgery 9: 25, 1941.
16. Rasmussen, R. A., Adams, W. E., and Hrdina, L. S.: Should the Pleural Space be Reduced in Size in the Resection of Lung Tissue? Surgery 10: 85, 1941.
17. Carlson, R. F., Charbon, B. C., Charbon, H. G. A., and Adams, W. E.: The Effect of Decreasing the Amount of Lung Tissue on the Right Ventricular Pressures in Animals, J. THORACIC SURG. 21: 621, 1951.

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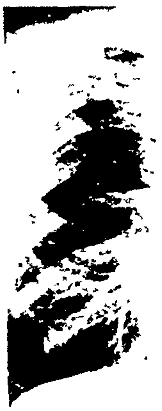

FUNCTIONAL CLASS IV.

T.L.C.	5.66 L.	
V.C.	2.5 L. (75%)	
R.V.	3.03 L.	
M.B.C.	32.0 L./min.(43%)	
1 sec V.C.	46%	
	Rest	Exer.
Pulm.Art.Press.	$\frac{75}{35}$(48)	$\frac{112}{45}$(67)
Art. O2 Sat.	96%	90%
Pulse Rate	84.0	92.0

J.S. 74 M.
7 1/2 yrs. post-left pneumonectomy

Fig. 12.—Case 8 (J. [illegible] of chest and data collected at cardiopulmonary evaluation on a 74-year- [illegible] ears after a left pneumonectomy. Note some lowering of pulmonary [illegible], however, a normal arterial oxygen saturation during rest. The pulmonary artery pressures in this patient were extremely high and became markedly elevated with moderate exercise. (Same key as in Fig. 10.) (From Harrison et al.[20])

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HONORED GUEST'S ADDRESS

NEW FINDINGS IN THE CORONARY-ENCEPHALIC PERFUSION IN DEPRESSED SURGICAL CASES

Alfonso Topete, M.D., Hector Huizar Lara, M.D., J. Trinidad Pulido, M.D., and Guillermo Diaz Caro, M.D., Guadalajara, Mexico

The great privilege of being requested to address, scientifically, this distinguished Society is an honor to me, to my country, and to my university.

I have accepted with modesty, not in the hope that my presentation may contribute much to scientific knowledge, but rather that this honor may serve as a stimulus to further experimentation and research among the young doctors of my country.

For this opportunity and recognition for my country, my colleagues, and myself, I am deeply grateful to Dr. William Adams, Dr. Langston, and the Committee that verified my nomination. Thank you.

The introduction of extracorporeal circulation and the progress attained in this field induced us more than 5 years ago to institute experiments related to the application of blood by perfusion to different parts of the body, in an effort to detect its possible therapeutic value in diverse pathologic conditions.

One of the studies which seemed to present possibilities and, therefore, has been continued in our laboratory pertains to the application of myocardial and encephalic perfusions in various acutely depressed states in which surgery is the only curative indication.

After extended animal experimentation the procedure was applied to human patients in an acutely depressed condition, due either to trauma, or to pathologic manifestations for which surgery was mandatory.

Finally, in the past year the procedure has been applied as a depression-preventive measure in surgical cases involving major risk.

This is a report of our experiences and findings to the present time in animals and human patients.

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18. Adams, W. E., Perkins, J. F., Flores, A., Chao, P., and Castellanos, M.: The Significance of Pulmonary Hypertension as a Cause of Death Following Pulmonary Resection, J. THORACIC SURG. 26: 407, 1953.
19. Sloan, H., Morris, J. D., Figley, M., and Lee, R.: Temporary Unilateral Occlusion of the Pulmonary Artery in the Preoperative Evaluation of Thoracic Patients, J. THORACIC SURG. 30: 591, 1955.
20. Harrison, R. W., Adams, W. E., Long, E. T., Burrows, B., and Reimann, A.: The Clinical Significance of Cor Pulmonale in the Reduction of Cardiopulmonary Reserve Following Extensive Pulmonary Resection, J. THORACIC SURG. 36: 352, 1958.
21. Webb, W. R., and Burford, T. H.: Studies of the Re-expanded Lung After Prolonged Atelectasis, A. M. A. Arch. Surg. 66: 801, 1953.
22. Weisel, W., and Jake, R. J.: Anastomosis of Right Bronchus to Trachea 46 Days Following Complete Bronchial Rupture From External Injury, Ann. Surg. 137: 220, 1953.
23. Mahaffey, D. E., Creech, O., Jr., and De Bakey, M. E.: Traumatic Rupture of the Left Main Bronchus Successfully Repaired Eleven Years After Injury, J. THORACIC SURG. 32: 312, 1956.
24. Forster, E.: Atelectasie pulmonaire prolongee et reversibilite functionelle, Lyon chir. 52: 484, 1956.
25. Portin, B. A., Rasmussen, G. L., Stewart, J. D., and Andersen, M. N.: Physiologic and Anatomic Studies Thirty-five Months After Successful Replantation of the Lung, J. THORACIC SURG. 39: 380, 1960.

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EXPERIMENTAL STUDIES[*]

To date the experiments have been performed on 525 dogs. These animals were subjected to massive blood loss by intubation of a large artery, either the abdominal aorta or the aortic arch, using a plastic tube introduced into the femoral or subclavian artery. The animals were subjected to bleeding and the spontaneous emptying of blood through the tube. Suction was then applied through the same tube to ensure maximum blood drainage. Blood loss was determined by radioactive means employing I^{131} and iodized albumin. By this method the volume of blood lost was estimated as 90 per cent in some animals and 95 per cent in others. It is noteworthy that to obtain this volumetric loss, suction was a requisite, as the large vessels mentioned spontaneously cease flowing when the volume of blood loss is between 60 and 70 per cent.

To avoid coagulation during this and subsequent steps, all animals received an intravenous dose of heparin, 2 mg. for each kilogram of weight, before arteriotomy. The temperature of the operating theatre was kept at a constant 27° C., which is our medial yearly temperature. In an attempt to avoid extraneous factors these experimental animals were treated as nearly as possible to a normal environment. Only one group, in which the thorax was opened, was anesthetized.

These animals were subjected to the following observations and controls: direct arterial pressure by intubation, electrocardiographic and electroencephalographic tests, body temperature control, blood chemistry and gasometric studies, and control of blood volume loss by the radioactive tests just mentioned.

After obtaining the maximum blood volume loss, oxygenated and heparinized blood, 18 mg. for each 500 c.c., was transfused immediately.

In 275 dogs the blood was introduced by coronary-encephalic perfusion as the initial step, followed by intravenous infusion. In the other group of 250 dogs the blood was introduced by intravenous or intra-arterial transfusion, both under pressure. The latter animals were used as a control group.

I. *Coronary-Encephalic Perfusion* (Fig. 1).—This procedure was used in 275 animals. A Sigmamotor pump was used with the Lillehei-DeWall apparatus. Later the De Bakey pump, employing the Kay-Anderson apparatus, was used, and more recently we have constructed a simple pump, using the De Bakey system. The blood was pumped through a plastic tube which had previously been introduced through a transverse incision in one of the femoral arteries and carried to the superior third of the descending thoracic aorta.

The amount of blood in each impulse was between 100 and 400 c.c., perfused at intervals. Once a normal or almost normal blood pressure level had been obtained by means of perfusion, the injection of blood was continued intravenously in the majority of dogs. In a few animals, intermittent perfusion was used to restore the blood loss.

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[*] The studies on shock verified by Blalock, Allen, Adams, Lillehei and others, have been used as the basis for this investigation. The word "depressed" is used in caution, considering the nature of our experiments, but we also use the word "shock" in our clinical cases.

In a group of 25 dogs treatment was administered exclusively by perfusion, the blood being totally replaced by this method. With this group the technique was changed. The perfusion was accomplished by means of a plastic tube with multiple small perforations in the portion which enters the abdominal region.

II. *Intravenous and Intra-arterial Transfusion Under Pressure.*—Two hundred and fifty animals were treated by these methods. The blood used was oxygenated and heparinized. A polyethylene tube, corresponding in size to a No. 18 needle, was introduced into a femoral vein or femoral artery for a length of 6 cm.

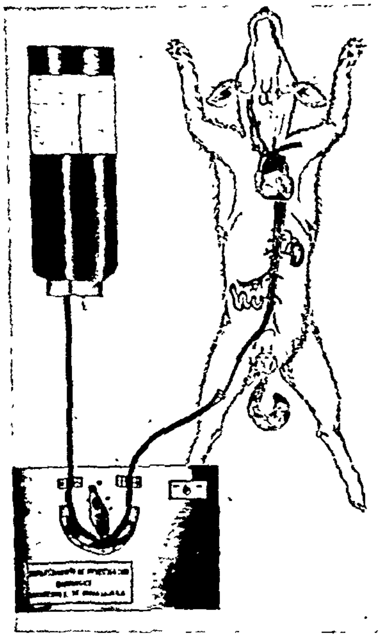

Fig. 1.

RESULTS

A comparison of survival and mortality results obtained to date in different groups and observations verified in experimentation follow.

Control Group.—

a. Treatment: Intravenous transfusion under pressure immediately after blood drainage; 132 animals were subjected to this procedure. Four animals, or 3.03 per cent, survived; 128 animals, or 96.07 per cent, died.

b. Treatment: Intra-arterial transfusion, immediately after blood drainage; 118 animals were subjected to this procedure. Six animals, or 5.08 per cent, survived; 112 animals, or 94.02 per cent, died.

Coronary Perfusion Group.—

a. Therapeutic application immediately after blood drainage; 200 animals were subjected to this procedure. One hundred and eighty animals, or 90 per cent, survived; 20 animals, or 10 per cent, died.

b. Therapeutic application between 1 and 2 minutes after blood drainage; 15 animals were subjected to this procedure. Eleven animals, or 79 per cent, survived; 4 animals, or 21 per cent, died.

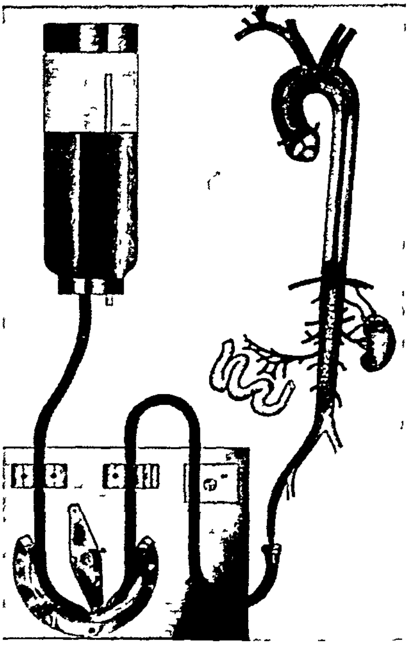

Fig 2.

c. Therapeutic application between 2 and 4 minutes after blood drainage; 20 animals were subjected to this procedure. Six animals, or 30 per cent, survived; 14 animals, or 70 per cent, died.

d. Therapeutic application between 4 and 6 minutes after blood drainage; 15 animals were subjected to this procedure. Two animals, or 10.3 per cent, survived; 13 animals, or 89.07 per cent, died.

It is interesting to note that none of these dogs, subjected to massive blood loss, presented ventricular fibrillation.

Exclusive Perfusion With Abdominal Multiperforated Tube (Fig. 2).—We consider our observations of this group incomplete. Taken into consideration was the problem of immediate abdominal irrigation achieved with the perfusion, so that the blood could pass to the intra-abdominal, coronary, and encephalic circulation, simultaneously.

The number of animals in this group is small in comparison with the other experiments, but to date there have been no deaths in the 25 dogs studied. Experiences relating to the measurement of coronary, encephalic, and intra-abdominal fluids are not reported, having been initiated recently and, are therefore incomplete.

Manometric Studies Relating to Blood Volume Loss Under I^{131} and Iodized Albumin Control.—

Volumetric losses of from 90 to 95 per cent were obtained in between 8 to 12 minutes. Arterial pressure dropped to 30 mm. Hg, although we consider the onset of depression to be when the volume of blood loss reaches 40 or 50 per cent. A pressure of zero was generally obtained when the animal had lost from 60 to 65 per cent of its blood volume. Some dogs presented heart arrest with very slow respiration when the loss of volume rose to 95 per cent. Several recovered spontaneously from the arrest when perfusion was applied.

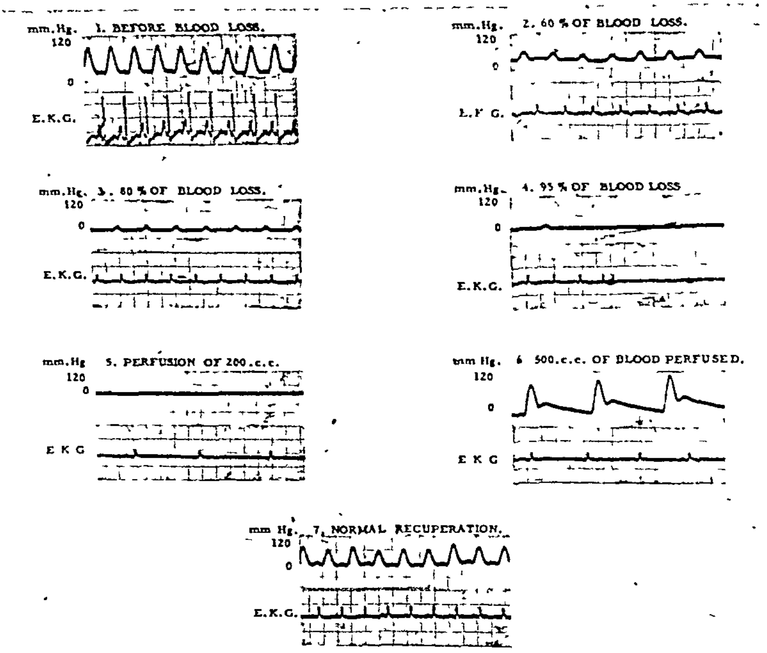

Fig. 3.

Electrocardiographic Studies (Fig. 3).—

The electrocardiogram generally demonstrates the abatement of the complexes when the volume of blood loss reaches 60 per cent. Inversions of T waves were observed when the hypotension was prolonged. The electrocardiogram tends to return to normal in relation to the increase of blood volume administered to the animal. The improvement observed with perfusion is remarkable, principally in the elevation of the complexes and stabilization of the T wave. We believe we have evidence that the electrocardiographic improvement is more conspicuous and rapid during perfusion than later after the blood has been totally restored.

Electroencephalographic Studies.—

The graphic decrease of the complexes during blood drainage, as relative horizontal is reached with a blood loss of 95 per cent, was clearly demonstrated.

As recuperation is initiated by perfusion, the electroencephalic curve also recovers with the rise in blood pressure.

Desoxycorticosterone Studies.—

When the systolic pressure of the animal reaches 30 mm. Hg, the desoxycorticosterone shows considerable elevation. Later, as the arterial pressure continues to drop, the desoxycorticosterone descends almost to zero. It rises again almost immediately when normal arterial pressure is re-established by the administration of blood. We have observed that, once the experiment is terminated and the arterial pressure totally restored by the replacement of blood, the desoxycorticosterone figure was always less than normal.

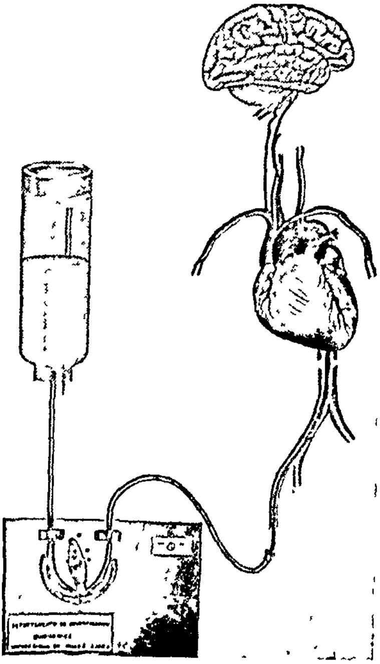

Fig. 4.

CLINICAL EXPERIENCE

To date, 50 patients have been treated in our surgical services. Perfusion was administered by means of a polyethylene or polyvinyl tube which was introduced into the first portion of the descending thoracic aorta through a transverse incision of one of the femoral arteries. In 2 cases, a transverse incision of the brachial artery was employed. All patients, even if hemorrhagic, were previously prepared by an intravenous injection of heparin, 2 mg. for each kilogram of weight. In some cases the blood was pumped with the Kay-Anderson pump, and in others our own pump was used. In 4 cases, because of special circumstances of an emergency character, we were obliged to use a 100 c.c. syringe to introduce the blood under pressure (Fig. 4).

In some cases ordinary citrated venous blood was administered and in others oxygenated and heparinized blood was used. Although to date it has not been possible to discover clinically any marked difference in the employment of these two methods, we have the impression from results obtained in animals that, in cases of grave depression, there may be some advantage in the use of oxygenated, heparinized blood.

The amount of blood used varied from 60 c.c. to 1,000 c.c. a minute, depending upon the case. The total quantity of blood used in a perfusion varied from 300 to 1,500 c.c. In all patients, intravenous transfusion of blood was continued after the arterial pressure rose to between 80 and 100 mm. Hg.

Patients treated in this manner have been divided into two groups.

Group I.—Acute: 28 patients in shock received treatment as follows: (a) traumatic emergency—5 cases, no deaths; (b) transoperative application—4 cases, no deaths; (c) postoperative application—14 cases, 1 death; and (d) post-partum application—5 cases, 1 death.

Perfusion was resorted to after venous transfusion, and, in 2 cases after arterial transfusion failed to obtain results. In 2 cases, one a post-partum hemorrhage and the other an injury of the subclavian artery, we were obliged to open the thorax and apply cardiac massage because of cardiac arrest. We believe the important factor in the recovery of both of these patients was that the massage, as well as perfusion, was applied in the course of the first few minutes after the onset of the arrest.

Of the 28 patients in group I, 2 died; one after a radical pelvic operation and one of a massive post-partum hemorrhage. In both instances shock had probably been present for some time. The post-partum patient was brought to the city 3 days after the mishap with symptoms of shock for the previous 6 hours.

After termination of the surgical procedure all patients of group I were treated with protamine, 2 mg. for each kilogram of weight.

Group II.—Preventive Application (Table I): We have used this method only during the past year. The procedure is applied to patients subjected to major surgical intervention in which the recognized risk of probable shock during operation exists, difficult to control by any means known at present. This situation is frequently complicated further by the precarious general condition of the patient which is due to a lifetime of nutritional deficiency. Surgical intervention was indicated for various pathologic processes: cancerous invasions; pleuropneumonectomy for destructive, toxic tuberculosis; massive intestinal resection for chronic conditions, such as extensive colectomies for ulcerative lesions with persistent hemorrhage, unresponsive to medical treatment, or extensive polyposis of the large intestine for which ample resection was indicated. The general condition of many of these patients was deplorable; presurgical preparation, although prolonged and including repeated blood transfusion, had proved unsatisfactory. This group was carefully selected, taking the shock control factor as the criterion. We have systematically refused preventive application of this method to patients who, although presenting a risk of shock during operation, have not been considered problems for control by the usual methods of blood transfusion.

TABLE I. PREVENTIVE APPLICATION

SURGICAL PROCEDURES	NO. OF CASES	DEATHS
Esophagectomies	3	0
Transthoracic gastrectomies	1	0
Pneumonectomies	3	0
Pleuropneumonectomies	2	0
Gastrectomies	4	0
Hysterectomies	4	0
Colectomies	3	0
Splenectomies	2	0
Totals	22	0

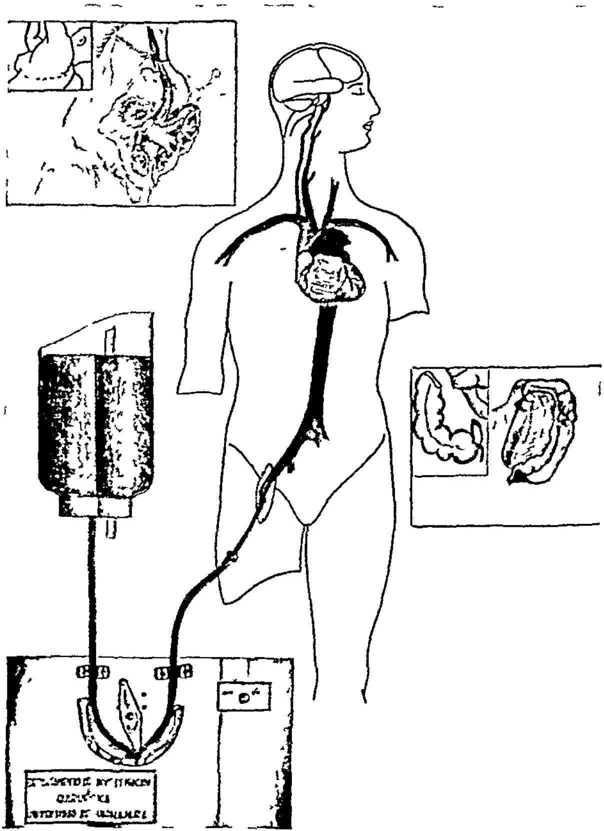

Fig. 5.

In no patient accepted was the systolic pressure higher than 90 mm. Hg after preoperative preparation. The ages varied from 23 to 60 years. The procedure used in these cases follows (Fig 5).

Before surgery, the patient received a dose of heparin 2 mg. for each kilogram of weight. This was followed immediately by a transverse incision in the femoral artery in the upper third of the thigh through which the plastic tube was introduced and passed to the descending thoracic aorta. This tube is connected to the pump tube, full of oxygenated, heparinized blood, 18 mg. of heparin for each 500 c.c. In some special cases citrated venous blood was transfused by means of a syringe. The surgical procedure was initiated. When arterial pressure dropped considerably we perfused from 80 to 150 c.c. of blood. Almost immediately in most cases, although in some there may be a delay of 2 or 3 minutes, the pressure rose until the preoperative figure was regained, or rose, in some cases, 10 to 20 mm. Hg higher. After return to normal pressure the application of venous blood was the usual procedure. The perfusion may be re-instituted as frequently as necessary when, and if, arterial pressure drops.

In the 22 patients studied with this technique, there has been no interruption of the surgical procedure, although in each of them perfusion has been applied at least four times. Three of these patients presented during surgery a systolic pressure reading below 50 mm. Hg eight different times during the operation. Perfusion was applied each time, using from 80 to 200 c.c. of blood.

Only in 2 cases did the quantity of blood applied both by perfusion and by vein reach 2,000 c.c.—1,000 c.c. by perfusion and 1,000 c.c. intravenously. In the remainder, the quantity of blood employed was between 1,000 and 1,500 c.c., the ratio remaining the same—half by perfusion and half by vein.

In 2 cases the blood was applied solely by perfusion. One of these was after a pneumonectomy in a 23-year-old married woman, mother of five, whose left lung was destroyed by tuberculosis with mediastinal deviation. After 5 months of preparation, based on specific medication and reconstructive therapy to improve her general condition, this patient was brought to surgery weighing thirty-eight kilograms, with an arterial pressure of 80 systolic and 60 diastolic. Massive introduction of blood was not feasible, yet the prevention of shock was imperative. Pneumonectomy was performed, only 800 c.c. of blood by perfusion being used during the procedure. After surgery, with a pressure of 100 systolic and 70 diastolic, the patient was given another half liter of blood; during the night another half liter was administered. Two months after surgery this patient is progressing satisfactorily.

The other patient had had a gastrectomy for ulcer and had received only 800 c.c. of oxygenated blood by perfusion during the surgical procedure.

All patients were treated with protamine sulfate, 2 mg. for each kilogram of weight, immediately after surgery. No bleeding complications occurred during or after the operations. There were no deaths in this group.

COMMENT

Studies carried out in our laboratories and clinical services during the past 5 years lead us to believe in the possibility of a new application of perfusions made available by extracorporeal circulation.

We believe that for years all of us have realized the advantages of a more effective use of blood transfusions for patients during surgical procedures or in shock. It is indisputable that the intravenous transfusion is a procedure to which humanity and the surgeon owes much; but we are also aware that intravenous transfusion frequently does not fulfill our requirements, and may even complicate certain situations—at times because of an excess of liquid, and again from the failure of direct action upon the cardiac muscle and encephalic centers. For an intravenous transfusion to reach these centers it is necessary for the blood to make a circuit throughout the body from the inlet, first passing through the cardiac cavities and the lungs, the myocardium and encephalon receiving no blood until after it leaves the left ventricle.

It may happen, especially in shock, that, because of the depressive condition itself, the right ventricle cannot eject or pump all the blood received by transfusion; the lungs cannot discharge the contained liquid and the left ventricle is also unable to pump properly. It is our belief that this condition is reflected in a decrease of the coronary and encephalic fluid, as has been demonstrated in many laboratories including ours. We have the firm belief that the tonicity and hemodynamic capacity of the ventricles should logically be elevated before these cavities receive a quantity of blood to be pumped immediately.

The first procedure which solved, in part, the problem of the blood reaching these centers in the form indicated was the intra-arterial transfusion. However, our experience, herein reported with the intra-arterial transfusion under pressure and transfusion by perfusion supports the premise that by the intra-arterial transfusion procedure a sufficient amount of blood does not reach the myocardium and encephalon. The idea of placing the plastic tube in the superior third of the descending thoracic aorta for the transfusion pumped has as its objective a major utilization of the fluid by these two centers. We believe that a short sound may be used, as in extracorporeal circulation, but in experiments we have made in animals, not herein reported, a much larger quantity of blood is required.

It is not our desire to circumscribe the therapeutics in these depressed states. We continue to believe that peripheral collapse is an important factor, which is the reason we also utilize venous introduction of blood or the abdominal multiperforated plastic tube in perfusion.

As we emphasized, from the experimental as well as from the clinical aspect the animals treated to date have been selected to emphasize the following: the animals were subjected to massive blood loss, subsequently treated by the introduction of blood, in part by ordinary methods, such as intravenous and intra-arterial transfusions, in part by coronary-myocardiac and encephalic perfusion. We believe more satisfactory results were obtained by the latter method. Clinically we observed two acute groups; one in which the usual methods employed would not have solved our problem, the other a preventive application group which contained patients who formerly would have been considered great operative risks or even inoperable.

It is our intention that this report be considered a review of our experimental investigations, interesting only in that it may be an indication for new techniques in the problem of utilization of blood in depressed states.

We extend our deep gratitude to Mrs. Lorraine Small de Chavez for her splendid cooperation.

Heparin (Liquemine) and protamine sulfate were kindly supplied by Hoffman-La Roche, Inc., Basilea, Switzerland.

REFERENCES

1. Adams, W. E., Thornton, T. F., Jr., Allen, J. G., and Gonzalez, D. E.: The Danger and Prevention of Citrate Intoxication in Massive Transfusions of Whole Blood, Ann. Surg. 120: 656, 1944.
2. Anderson, R. M., Anderson, D. P., and Kay, J. H.: A Filmer: For the Stationary Screen Oxygenator, Surgery 42: 896-897, 1957.
3. Blalock, A.: Principles of Surgical Care, St. Louis, 1940, The C. V. Mosby Company.
4. Cohen, M., Warden, H. E., and Lillehei, C. W.: Physiologic and Metabolic Changes During Autogenous Lobe Oxygenation With Total Cardiac By-Pass Employing the Azygos Flow Principle, Surg. Gynec. & Obst. 98: 523, 1954.
5. De Wall, R. A., Warden, H. E., Gott, V. L., Read, R. C., Varco, R. L., and Lillehei, C. W.: Total Body Perfusion for Open Cardiotomy Utilizing the Bubble Oxygenator: Physiologic Responses in Man, J. THORACIC SURG. 32: 591, 1956.
6. Einheber, A., Lillehei, R. C., and Clarke, R. W.: Hemorrhagic Shock in Dogs, Am. J. Physiol. 183: 611, 1955.
7. Green, D. M., and Metheny, D.: The Estimation of Acute Blood Loss by the Tilt Test, Surg. Gynec. & Obst. 84: 1045, 1947.
8. Kay, J. H., and Gaertner, R. A. A.: Simplified Pump Oxygenator With Equal to Normal Cardiac Output, S. Forum 18: 267-271, 1957.
9. Necheles, H., Levinson, O., Janota, M., and Arimoto, F.: Pre-Infusion—A Study in the Prevention of Hemorrhagic Shock, Surg. Gynec. & Obst. 42: 499, 1955.
10. Lam, C. L.: Cardiovascular Surgery, Philadelphia, 1955, W. B. Saunders Company.
11. Seldon, T. H.: The Importance of Blood in Preoperative and Postoperative Treatment, Surg. Gynec. & Obst. 84: 1124, 1947.
12. Topete, A., Pulido, J. T., and Huizar, H.: Recientes Avances en el Estudio Físio-Patológico del Shock Quirúrgico, XI Asamblea Nacional de Cirujanos, Mexico, 1956.
13. Topete, A., Pulido, J. T., Huizar, H., Steves, A., and Castellanos, G. L.: Perfusion Coronaria, masaje cardíaco y transfusion en el tratamiento del Shock Quirúrgico-oligo hemico, Bull. Soc. Internat. Chir. 17: 122-130, 1958.
14. Wiggers, C. J.: Physiology in Health and Disease, Philadelphia, 1949, Lea & Febiger.

TERATOID TUMORS OF THE MEDIASTINUM FOUND DESPITE PREVIOUS NORMAL CHEST RADIOGRAPHY

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We present 2 patients with large teratoid tumors of the mediastinum, which were successfully removed 2 and 4 years after chest radiographs, taken for routine purposes, had shown no abnormality.

CASE REPORTS

CASE 1.—J. A. was admitted to Victoria Hospital, Blackpool, on July 16, 1954, when she was 21 years of age. She gave a history of left chest pain, fever, and effort dyspnea for 1 month before admission; toward the end of this time a small cystic swelling appeared at the sternal notch (Fig. 1) which, on aspiration, was found to contain opaque fluid containing large numbers of cholesterol crystals, but no pus cells or organisms, and was sterile on culture. There was no significant previous medical history. A chest radiograph, taken as a condition of her employment 2 years previously, had been normal (Fig. 2).

On admission to hospital, chest radiography revealed a large mass projecting from the anterior mediastinum into the left hemithorax (Fig. 3). The heart was greatly enlarged, and, on screening, pulsation was diminished, suggesting a pericardial effusion. At left thoracotomy (July 28, 1954; J. S. G.), a large mass with a smooth surface was seen to be confluent with the pericardium and the mediastinum. The pericardium was distended and 100 c.c. of hemorrhagic fluid were removed by aspiration. The main mass was punctured and some yellowish granular material with thin, apparently purulent, fluid escaped. The mass was firmly adherent to the mediastinum, and was dissected with difficulty. The patient's postoperative recovery was uneventful, and subsequent chest radiographs have been normal.

Macroscopic examination showed a large cyst, measuring 12 by 11 cm., with flakes of bright yellow material adherent to the inner lining. The wall was thickened and fibrosed; the cavity was unilocular showing two or three large pockets containing bright yellow material. There were two prominent masses of tissue covered with normal skin and hair projecting from the inner lining, probably mammillae. A section of one of these showed a central core of fat covered with skin; a second mass at the base also contained skin. A section of the wall, which was 1 cm. thick, showed marked fibrosis with bright yellow foci.

Microscopic examination of a section of the wall showed skin, sebaceous gland, and hair follicles. In the deeper part of the wall there were areas of adipose tissue, lymphoid tissue, plain muscle fibers, cartilage, mucus and mixed glands, and one large space was lined with respiratory pseudostratified ciliated epithelium (Fig. 4, *A* and *B*). There was no evidence of malignancy or of inflammatory change.

Diagnosis.—Benign cystic teratoma of the mediastinum.

From High Carley Hospital, Ulverston, and Victoria Hospital, Blackpool, England.
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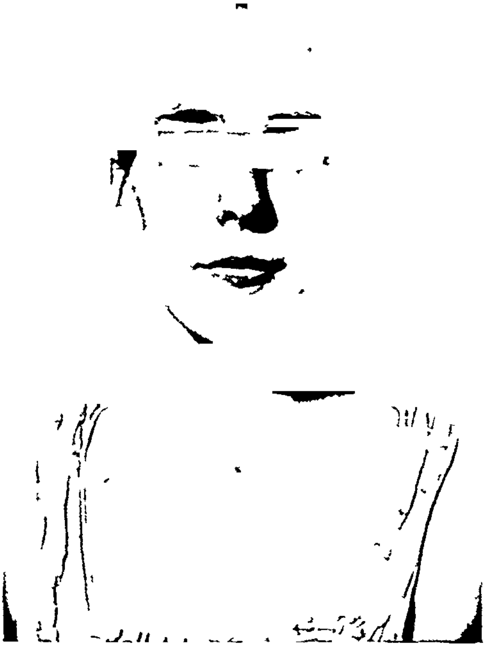


Fig 1—Case 1 The swelling in the suprasternal notch is shown

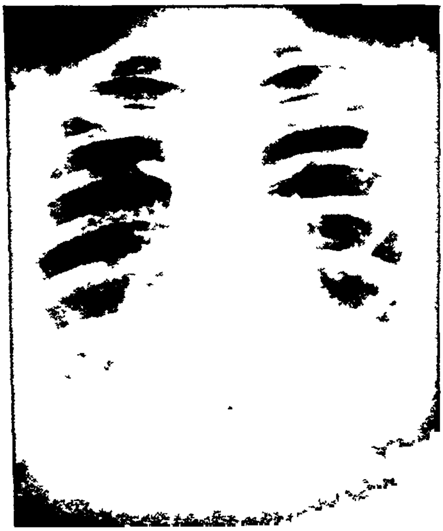


Fig 2—Case 1 Miniature chest radiograph of July, 1952, was considered normal

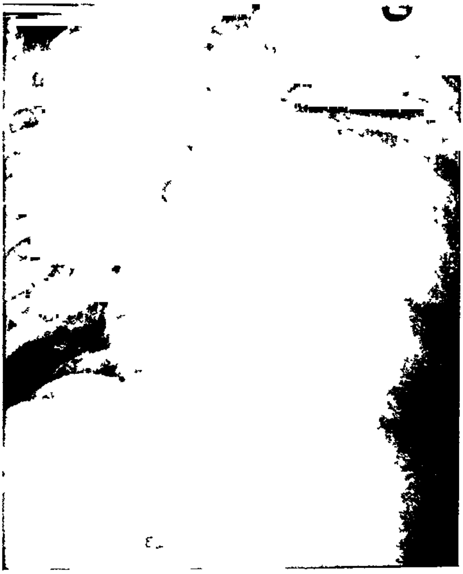
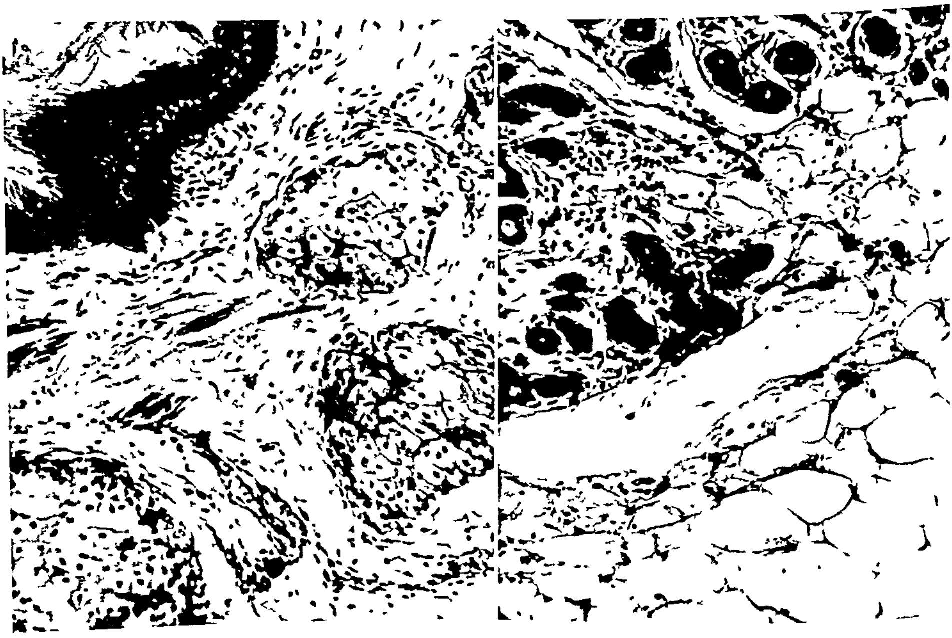


Fig 3—Case 1 Posteroanterior chest radiograph made in July, 1954



A

B.

Fig. 4—Case 1 A and B, Photomicrographs (high power and hematoxylin and eo stain) which show sebaceous glands, respiratory pseudostratified epithelium, adipose tiss and mucus and mixed glands

CASE 2.—J. P., a 37-year-old foreman shipwright, was admitted to High Carley Hospital on June 16, 1958, with a history for the previous 6 months of intermittent substernal pain, sometimes referred to the right side of the neck and brought on by bending or twisting. He was otherwise free of symptoms. There was no relevant previous medical history; a miniature radiograph taken in November, 1954, was normal. On admission to hospital, a chest radiograph showed a dense lobulated well-defined shadow in the right mid and lower zones (Fig. 5, *A*), and seen on the lateral view to lie anteriorly (Fig. 5, *B*) and continuous with the mediastinum.

At right thoracotomy (July 16, 1958; J. S. G.), a large anterior mediastinal tumor was found, which did not involve the lung. This was shelled out without difficulty, and the patient's postoperative course was uneventful. He has since remained free of symptoms and his chest radiograph is normal.

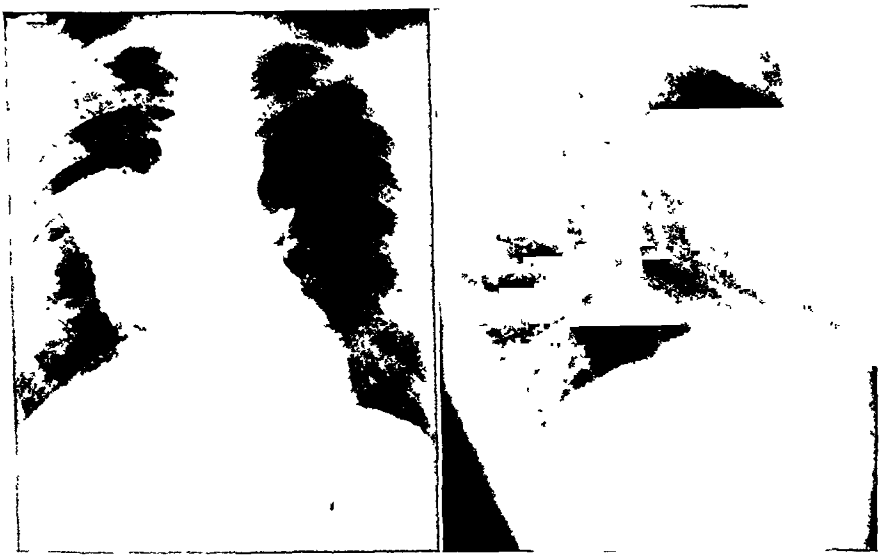


FIG. 5.—Case 2 Lateral chest radiograph *(A)* and posteroanterior chest radiograph *(B)* made on June 13, 1958.

Macroscopic examination showed an encapsulated tumor of ovoid shape, weighing 290 grams (Fig. 6). It was smoothly encapsulated, but the capsule was roughened by adherent pieces of pleural membrane. It measured 10 by 7 by 8 cm. The cut surface showed a variegated multicystic pattern; the cysts were small, the maximum measuring 1.5 cm. in diameter. Many of the cysts were filled with coagulated mucus and others contained watery fluid. The firm tissue varied markedly in consistency and color. In some areas there was a marked lipoid element; other parts were composed of very white soft tissue suggestive of cerebrum, but others were of much firmer nondescript material. The appearance was typical of dermoid tumor.

Microscopic examination (Fig. 7, *A* and *B*) of the tumor showed a capsule of thick fibrous tissue, rich in blood vessels. The tumor itself was composed of a multiplicity of tissues which had reached an adult form of development, apart from occasional areas showing less well-differentiated tissue; for example there was one piece looking very like embryonic lung epithelium. The following structures could be identified; skin; sebaceous glands and hair follicles; respiratory epithelium; embryonic lung tissue and cartilage; nerve, brain, and choroid; smooth and striped muscle, fat, vascular channels, and lymphoid follicles. The tumor was histologically benign.

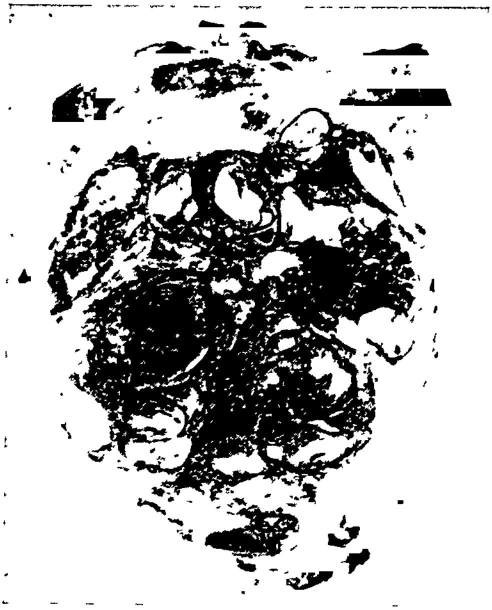
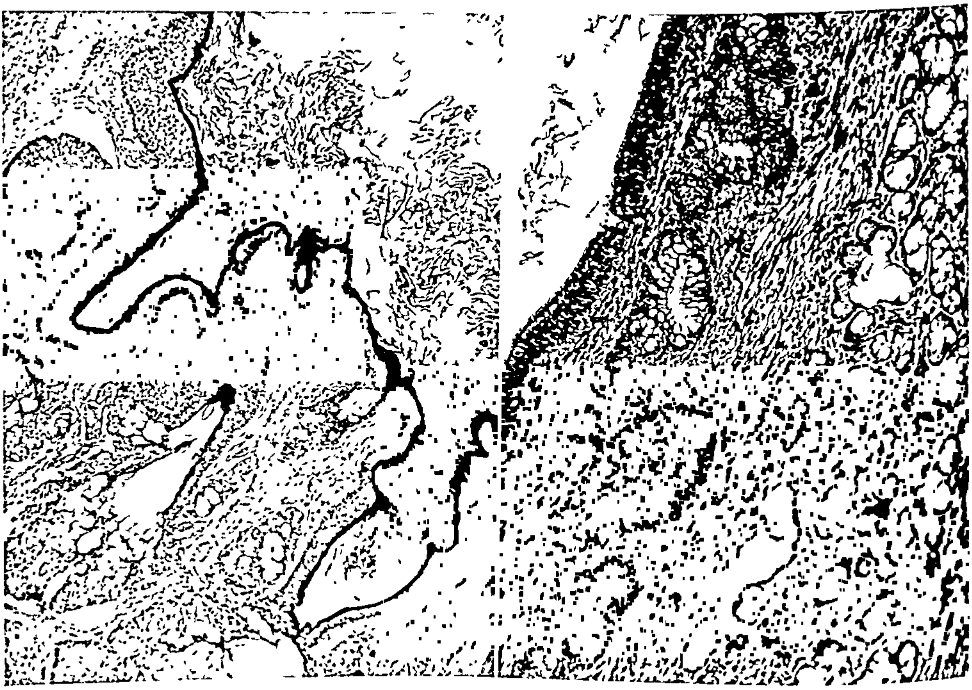


Fig. 6.—Case 2. Macroscopic picture of specimen which shows multiple small cysts.



A. *B.*

Fig. 7.—Case 2. *A* and *B*, Photomicrographs which show multiplicity of tissues which compose the tumor.

DISCUSSION

Rusby[3] reviewed 245 cases of teratoid tumor from the world literature and added 7 of his own. He referred to the importance of an increase in size of a teratoid tumor as an urgent indication for surgical resection, in view of the possible development of malignancy. Eleven and nine-tenths per cent of the 252 cases proved to be malignant, although this change was not necessarily associated with a recognized increase in size.

More recently, Morrison[2] found 36 teratoid tumors in a series of 332 cases of tumors and cysts of the mediastinum; 3 of 36 were malignant.

We have been unable to find any reference in the literature to the development of evidence of a teratoid tumor after previous chest x-ray studies had been normal; our 2 cases demonstrate that this diagnosis is not in fact excluded by a previous normal radiograph.

The cause of the quite rapid enlargement of the tumors remains a matter for speculation. It must be assumed that an embryological rest was present at the time of the normal radiograph; yet after an interval of only 2 years, the first patient showed evidence of a cystic tumor measuring 12 by 11 cm., while in a second patient, a tumor, measuring 10 by 8 by 7 cm., had developed after a 4-year interval. The first tumor contained one large cystic space, while the second contained numerous small cysts and much solid tissue.

In neither tumor was there any evidence of malignancy or of acute infection, and it seems that the accumulation of fluid in the cystic spaces accounted for only a proportion of the enlargement noted.

Willis[4] points out that in a small proportion of mediastinal teratomas, the pericardium is involved, as in our Case 1, and adds that the majority of these patients present symptoms in infancy or childhood. Discussing the maturation of tissues in teratomas, he says, "Malignant teratomas contain embryonic tissues of varying degrees of immaturity, often along with maturing and well-differentiated ones. The mixture of differentiating tissues of all ages is one of the most striking features of actively growing teratomas. Now, while the presence of immature tissues in a teratoma in an adult is clear evidence of its continued proliferation and probable malignancy, this does not necessarily apply to a similar growth in a foetus or young infant, whose own normal tissues are themselves still immature." The lack of evidence of malignancy in our cases is notable, although some immature tissue was found in the specimen of Case 2.

The appearance of a cystic swelling in the suprasternal notch in Case 1 appears to be somewhat unusual, although Hedblom[1] refers to 19 similar instances collected from the literature.

SUMMARY

Two patients are described from whom large teratoid tumors were removed 2 years and 4 years after a routine chest radiograph had proved to be normal. There was no evidence of malignancy or of acute inflammation in either tumor, and the cause of the rapid increase in size remains a matter for speculation.

Our thanks are due to Dr. A. A. Miller for the report on the specimen on Case 1, and to Dr. A. Rickards for the report on the specimen on Case 2.

REFERENCES

1. Hedblom, C. A.: Intrathoracic Dermoid Cysts and Teratomata With Report of 6 Personal Cases and 185 Cases Collected From the Literature, J. THORACIC SURG. 3: 22, 1933.
2. Morrison, I. M.: Thorax 13: 294, 1958.
3. Rusby, N. L.: Dermoid Cysts and Teratomata of Mediastinum; Review, J. THORACIC SURG. 13: 169, 1944.
4. Willis, R. A.: The Borderland of Embryology and Pathology, London, 1958, Butterworth & Co., Ltd., p. 440.

ESOPHAGOPLEURAL FISTULA AS A COMPLICATION OF THORACIC SURGERY

A Collective Review

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Takeshi Okano, M.D., Oteen, N. C.

THE appearance of an esophagopleural fistula following thoracic surgery for nonmalignant disease has been rarely reported in this country; only four instances have been recorded to our knowledge.[1-3] When 2 patients with esophagopleural fistulas were treated simultaneously in our hospital recently, it occurred to us that perhaps this complication was not, in fact, as rare as the paucity of reports seemed to indicate. The purpose of this review is to show that this complication has followed thoracic surgical procedures in a good many centers in this country. It is hoped that analysis of all available cases may throw some light upon the pathogenesis of this distressing condition and may serve as a guide for treatment and, if possible, for prevention.

A questionnaire was prepared and mailed to 122 thoracic surgeons in the United States and to 1 in India, regarding the development of esophagopleural fistulas in association with thoracic surgery. Replies were received from 69 surgeons, 28 of whom answered affirmatively and contributed clinical material for this study.

Data on 33 cases of esophagopleural fistula following intrapleural* surgical procedures thus became available for review. Twenty-four of these followed a pneumonectomy, all but three occurring on the right side. Five followed lobectomies of various kinds. Single instances of fistulas occurred following hiatus hernia repair, thoracic aneurysm resection, removal of bronchogenic cyst, and lysis of adhesions during intrapleural artificial pneumothorax were also reported.

PATHOGENESIS

The primary disease was pulmonary tuberculosis in 22 of these patients and suppurative disease in 6. A bronchial adenoma accounted for a single case, and the hernia, the aneurysm, and the bronchogenic cyst accounted for 3 others. In one instance, the etiology of the primary disorder was unknown to us.

From the Veterans Administration Hospital, Oteen, N. C.

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*The word "intrapleural" is used for the sake of simplicity, to distinguish these operations from those purely chest wall extrapleural procedures, such as thoracoplasty or extrapleural pneumonolysis. A small number of extrapleural pneumonectomies or pleuropneumonectomies are included in this "intrapleural" group.

In 16 cases, the fistula was diagnosed within 3 months of surgery (within 1 month in 10 cases). Operative injury to the esophagus was recognized at surgery or autopsy in 5 of these patients. In 3 others it was noted that the esophagus was intimately related to the lesion being resected, but no injury was recognized. The surgical procedure was difficult in at least 5 other cases, a pleuropneumonectomy or a completion pneumonectomy (following a previous lesser resection) being the operation performed. One can assume with some assurance that surgical trauma contributed directly to the development of esophagopleural fistula in most of these 16 cases. The primary disease was tuberculosis in only half of them (50 per cent).

In the remaining 17 cases, the fistula was diagnosed from 3 months to 6 years following the major thoracic operation, save for 1 case in which there was incomplete data on this point. In these 17 patients, the primary disease was pulmonary tuberculosis in 14 (82 per cent). At least 11 were known to have developed a bronchopleural fistula and/or empyema postoperatively. Thus, chronic infection almost certainly played a major role in most instances in this group.

INCIDENCE

One suspects that this complication occurs much more commonly than the scanty reports in the literature would indicate. Nearly half of the 69 surgeons who sent replies to our questionnaire were able to report cases of this complication—in some instances, several cases. At the Veterans Administration Hospital in Oteen, North Carolina, during the past 12 years, 4 cases were seen in a group of 934 resections for pulmonary tuberculosis. Most of the total of 33 cases collected occurred in the past 5 years.

CINICAL PICTURE AND DIAGNOSIS

There appears to be no typical clinical picture of the development of this complication. The onset was commonly more abrupt in instances in which the fistula occurred soon after surgery, and more insidious in later-appearing fistulas. Symptoms developing soon after surgery often suggested the clinical picture of a bronchopleural fistula or empyema. Fever and chest pain usually occurred at the onset–subcutaneous emphysema, occasionally. The finding of food particles or previously ingested fluid in pleural drainage was commonly the first sign of the presence of a fistula, and is pathognomonic. It was usually readily verified by the observation in pleural drainage of previously ingested methylene blue, or by the ingestion of barium or Lipiodol, and radiography. Severe weight loss and even emaciation were features in some of the chronic cases, but these were not constant.

The level of the fistula, as identified roentgenographically or at autopsy, was in the mid-esophageal area at or near the tracheal bifurcation in 15 patients who underwent resection for tuberculosis, and in 4 others who had nontuberculous conditions (Fig. 1). There were four fistulas in the lower third of the esophagus in tuberculous patients, and four in nontuberculous cases. In the remainder, the level of the fistula was not identified

TREATMENT AND RESULTS

Treatment was varied, and complicated, with multiple procedures in many patients. This makes analysis somewhat difficult. In general, however, direct attacks on the fistula, by suture or by muscle-implants in 8 patients led to partial or complete success in 7, with one death. Four attempts to reconstruct an esophagus from segments of colon, jejunum, or stomach resulted in fatalities. In 10 patients, only chest wall surgery, including drainage, Schede thoracoplasty, etc., were performed as definitive treatment, with two deaths. In 10 others, definitive surgical treatment (other than jejunostomy or gastrostomy in some) was not carried out. In this group there were nine deaths. The over-all mortality rate was 49 per cent.

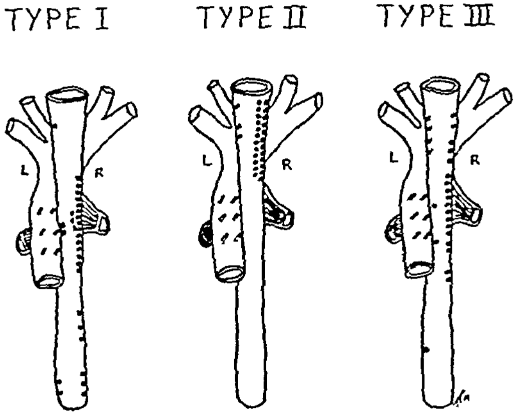

Fig. 1.—Diagram indicating approximate level and side on which 81 esophagopleural or extrapleural-esophageal fistulas occurred. *Type I:* Fistulas following intrapleural operations, but including also extrapleural pulmonary resections. *Type II:* Fistulas following extrapleural operations such as thoracoplasty and extra pleural pneumonolysis, but not including extrapleural pulmonary resections. *Type III:* Fistulas following chronic empyema not associated with major thoracic surgery.

Complete cure, with no residual sinus, empyema space, or fistula, was achieved in only 5 tuberculous patients. Chest wall surgery of the Schede thoracoplasty or sinus excision type was performed in 2 cases, and in combination with these procedures, a muscle flap operation, direct closure of the fistula and excision and re-anastomosis of the esophagus, were successful in the other 3. One nontuberculous patient was successfully treated with closed suction drainage and another by thoracoplasty. The primary disease in the latter was not known to us. The over-all cure rate was 21 per cent. The remaining survivors retained a draining sinus, fistula, or empyema space. These data are summarized in Tables I, II, and III.

CASE REPORTS

CASE 1.—C. M., a 37-year-old white man, was admitted to the VA Hospital at Oteen, North Carolina, in 1949 for closure of a Monaldi cavernostomy.

In 1944, the patient had had resection of a mediastinal neurofibroma from the right paravertebral gutter at the fourth thoracic vertebral level, which was "pressing on the esophagus." Recovery was apparently uneventful. The onset of pulmonary tuberculosis

TABLE I

CASE NO.	MAJOR OPERATION PRECEDING FISTULA	OPERATIVE AND POSTOPERATIVE COURSE	INTERVAL BETWEEN OPERATION AND DIAGNOSIS OF FISTULA	TREATMENT	RESULTS
A. Esophagopleural Fistulas Following Resections for Pulmonary Tuberculosis					
1	Right pleuropneumonectomy	BPF; thoracoplasty	17 months	Jejunostomy; Schede thoracoplasty	Cured
2	Right pleuropneumonectomy	BPF; empyema; rib resection	7 weeks	Gastrostomy; direct closure (failed), resection and end to end anastomosis	Cured
3	One prior resection; completion right pneumonectomy	Difficult operation; empyema; open drainage	3 weeks	Gastrostomy; cautery	Fistula persists
4	Prior resection and thoracoplasty; completion left pneumonectomy	BPF; Schede thoracoplasty; spread	8 months	Jejunostomy	Died; extensive tuberculosis remaining lung
5	RUL; superior segment, RLL; Wedge, RML	Empyema; thoracoplasty; open drainage; Schede	3 years	Gastrostomy twice; laparotomy (intussusception)	Died; gastrojejunal fistula
6	Prior resection and empyema; completion right pneumonectomy	Difficult operation; intrapericardial ligation of torn pulmonary artery	Less than 2 months	Gastrostomy thoracoplasty; secondary bronchial closure; jejunal bypass operation	Died
7	Prior resection and BPF; completion left pneumonectomy	BPF; empyema	17 months	Gastrostomy	Died soon after gastrostomy
8	Right pleuropneumonectomy	Empyema; rib resection	6 years	Gastrostomy; 2 stage thoracoplasty	Alive with gastrostomy
9	Right pneumonectomy	Oleothorax established postop.	2½ years	Gastrostomy; open drainage	Died 3 months after diagnosis
10	Right pleuropneumonectomy	Extensive dissection	8 months	Gastrostomy; Schede thoracoplasty, skin graft	Alive and working; fistula persists 6 years
11	Right pleuropneumonectomy	BPF; Schede thoracoplasty; muscle flap	2½ weeks	--	Died 5 days after fistula diagnosed
12	RU lobectomy and RM lobectomy	Empyema; open drainage; thoracoplasty	Approximately 1 year	--	Died; condition too poor for surgery
13	Pneumonectomy	Empyema	Few days	--	Died; autopsy: esophageal injury unrecognized at surgery
14	Right pleuropneumonectomy	Empyema—drained	7 days	Gastrostomy; jejunostomy; thoracoplasty; Schede thoracoplasty; several attempts at direct repair; colon bypass	Died—complete separation of both anastomoses

15	*Right pneumonectomy*	3-stage thoracoplasty	18 months	Fistula excised; wall of esophagus closed	Alive, fistula reopened, closed
16	Two prior resections; completion, right pneumonectomy plus pleurectomy	Localized empyema found at operation; esophagus carefully identified	4 days	Closed, then open drainage	Alive; drainage continuing 1 mo. postop.
17	Right pneumonectomy	BPF; empyema	11 months	--	Died 2 mo. after diagnosis
18	Prior resection, mediastinal tumor; prior 3-stage thoracoplasty plus Monaldi; right pneumonectomy	Difficult operation, BPF; empyema; rib resection	22 weeks	Jejunostomy; Schede thoracoplasty	Alive; fistula closed; 6 year follow-up
19	Left pneumonectomy	Difficult operation; BPF; empyema, open drainage	16½ months	Tube feedings only	Died, cavitary disease, opposite lung
20	Prior resection and thoracoplasty; completion right pneumonectomy	Esophagus mobilized inadvertently; empyema; open drainage	20 weeks	Schede thoracoplasty and revisions	Died 2½ years later
21	Prior resection; 3-stages of thoracoplasty; completion, right pneumonectomy	Lung densely adherent; febrile postop. course	12 weeks	Open drainage; Schede thoracoplasty and revisions	Alive; fistula persists 2½ years
22	Intrapleural lysis of adhesions, left	--	--	Gastrostomy; thoracoplasty; muscle flap	Recovered
	B. Esophagopleural Fistulas Following Operations for Nontuberculous Disease				
23	Removal of bronchogenic cyst	Esophagus stretched over cyst	5 weeks	Gastrostomy; rib resection; decortication plus pleural flap	Alive; residual sinus
24	Suppurative disease; right pneumonectomy	BPF	3 weeks	Pleural flaps (failed); 2-stage thoracoplasty	Alive; residual empyema
25	RML and RLL for bronchiectasis	Difficult operation	11 days	Tube feedings; closed drainage	Recovered
26	Repair of hiatus hernia	--	6 days	Primary repair failed Esophagogastrostomy failed	Died
27	RML and RLL for bronchiectasis + cysts	Esophagus injured	5 days	Tube feedings	Alive; residual empyema, 7 years
28	RU lobectomy for lung abscess	Esophagus injured; empyema	10 weeks	Multiple Schede operations	Alive; residual space
29	Pneumonectomy	--	9 months	Thoracoplasty	Recovered
30	Resection, aortic aneurysm	Esophagus injured; repaired at initial operation	5 days	--	Died
31	Right pleuropneumonectomy for lung abscess	Abscess opened at operation	3 years	Gastrostomy; rib resection; cautery	Alive; fistula persisted
32	Right pneumonectomy for bronchial adenoma	BPF; bronchus resutured with wire	1 month	--	Died; wire suture eroded esophagus
33	Right pneumonectomy for lung abscess	Difficult operation	2 years	Gastrostomy; empyema drainage; 2 attempts to repair; colon bypass operation	Died; bypass operation unsuccessful

Notes: Case 1—Ref. 2; Case 2—Ref. 3; Cases 3-17—contributed (see acknowledgments); Cases 18-21—VA Hospital, Oteen, N. C.; Case 22—Ref. 63; Cases 23 and 24—Ref. 1; Cases 25-33—contributed (see acknowledgments).

Abbreviations: BPF—bronchopleural fistula. RUL—right upper lobectomy. RML—right middle lobectomy. RLL—right lower lobectomy.

TABLE II. ETIOLOGY AND DIAGNOSIS, NONMALIGNANT ESOPHAGOPLEURAL FISTULAS

TYPE OF FISTULA	ETIOLOGY OF PRIMARY DISEASE				INTERVAL BETWEEN SURGERY (OR EMPYEMA)* AND CLINICAL DIAGNOSIS OF FISTULA	
	PULMONARY TUBERCULOSIS	NONTUBERCULOUS DISEASE	UNKNOWN	TOTAL	LESS THAN THREE MONTHS	MORE THAN THREE MONTHS
I. Following intrapleural thoracic surgery	22	10	1	33	16	17
II. Following extrapleural thoracic surgery	33	0	0	33	4	29
III. Following empyema not associated with thoracic surgery†	10	20	5	35	14‡	15‡
Totals	65	30	6	101	34	61

*Applies only to Type III fistulas

†Except drainage operations.

‡Data incomplete.

TABLE III. TREATMENT AND RESULTS, NONMALIGNANT ESOPHAGOPLEURAL FISTULAS

TYPE OF FISTULA	MANAGEMENT				OVER-ALL MORTALITY RATE	OVER-ALL CURE RATE‡
	PRIMARILY SURGICAL*		PRIMARILY MEDICAL†			
	NUMBER OF PATIENTS	DEATHS	NUMBER OF PATIENTS	DEATHS		
I.	22	6	10	9	49%	21%
II.	22	11	11	7	55%	19%
III.	12	4	24	14	51%	41%
Totals	56	21 (38%)	45	30 (67%)	51%	27%

*Thoracic surgery on chest wall or mediastinum, with and without gastrostomy or jejunostomy.

†With and without gastrostomy or jejunostomy

‡Survivors with no residual fistula, sinus, or empyema space

was in 1948, with bilateral disease, cavitary on the right. An anterior thoracoplasty and cavernostomy followed by two-stage posterolateral thoracoplasty were done at another hospital.

Soon after admission to Oteen, revision of the draining fistula in an attempt to close it was unsuccessful. Because of continuing positive sputum for acid-fast bacilli the presence of a residual cavity under the thoracoplasty, and the draining cavernostomy, pneumonectomy was undertaken on Feb 6, 1951. The operation was difficult. There was gross pleural contamination in cutting across the fistulous tract. The specimen contained caseocavernous lesions of tuberculosis Approximately 2 weeks later, a bronchopleural fistula and tuberculous empyema were drained by a wide open thoracotomy, resecting portions of five ribs. Five months later, food and fluid were noted to be draining from the thoracotomy wound. A pleuroesophageal fistula at the level of the sixth and seventh thoracic vertebrae was confirmed by barium swallow (Fig. 2). Since Levine tube feedings did not function well, a Witzel jejunostomy was done, and a modified Schede thoracoplasty to obliterate the space was carried out. Four months after discovery of the fistula, no more food or fluid was noted to be draining from the chest, and in another 2 months the pleural space had completely been obliterated. Nutrition had been fairly well maintained, the minimum weight (93 pounds) being about 30 pounds below the pre-pneumonectomy weight. At his discharge 10 months after the fistula appeared his weight was 116 pounds.

He was seen again 6 years later, still thin, but fairly active. The right chest wounds had remained healed. Cold fluids produced a cold sensation over the thin skin covering the right mediastinum and chest wall. A barium swallow still showed marked diverticulum formation at the same level as noted 7 years earlier (Fig. 3).

CASE 2.—S. J. M., a 33-year-old white man, was admitted to the VA Hospital at Oteen, North Carolina, in June, 1953, for the treatment of pulmonary tuberculosis. The onset of his disease was in 1950 and was characterized by bilateral disease, with a 6 cm. cavity in the left upper and a 3.5 cm. cavity in the left lower lung fields. On Oct. 29, 1953, left pneumonectomy was carried out, in part by extrapleural dissection. The operation was difficult because of distortion due to marked mediastinal shift to the left, and dense adhesions. According to the surgeon's note, "Some difficulty was encountered in finding the inferior pulmonary vein until it was realized that the heart had shifted over and dissection was being carried out over the left auricle."

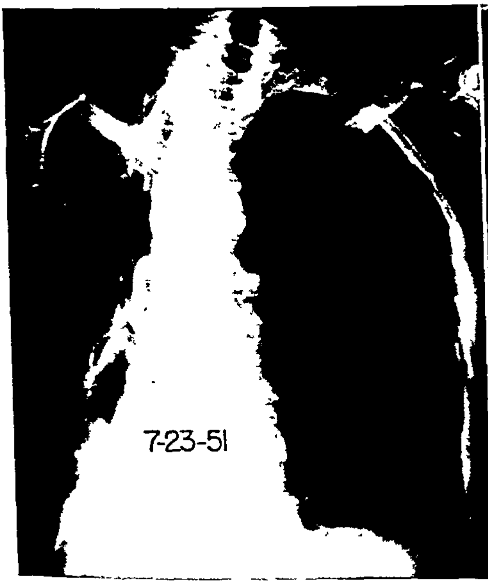

Fig. 2.

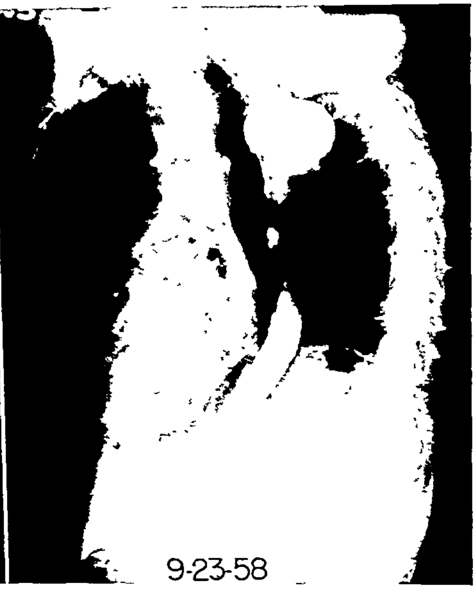

Fig. 3.

Fig 2.—Case 1. Mid-esophageal fistula opening into right pleural space diagnosed 22 weeks following right pneumonectomy which was complicated by the development of a bronchopleural fistula and tuberculous empyema. The fistula healed 4 months later, following modified Schede thoracoplasty.

Fig. 3.—Case 1. Esophageal deformity just proximal to the site of the fistula, 7 years later. Patient asymptomatic. Similar deformity was noted on this view 7 years earlier.

An empyema and bronchopleural fistula developed 3 weeks postoperatively which required first closed, then open, thoracotomy. In spite of drainage, the patient remained febrile and 8 weeks following the resection, unexplained spiking elevations of temperature were noted. Cultures from the empyema drainage were positive for acid-fast bacilli. There was no evidence of reactivation of disease in the opposite lung. Drainage and fever continued unabated for 6 months, and the patient's condition was deemed too poor for him to undergo thoracoplasty. Viomycin was added to his drug regime and he gradually improved, the empyema space diminishing in size. The bronchopleural-cutaneous fistula remained open. There was an episode of syncope in June, 1954. From July until December, 1954, the patient was afebrile. Thereafter elevation of temperature recurred again, ranging from 99° to 102° F. daily.

On March 9, 1955, 16 months following the resection, food and water were noted on his dressings for the first time. A barium swallow demonstrated the presence of an esophagopleural-cutaneous fistula at the mid-esophageal level. In spite of tube feedings and parenteral fluid therapy, there were episodes of cyanosis due to regurgitation of secretions and fluids through the fistula into the remaining lung. The patient continued to lose ground and died 4 months after the fistula was discovered.

At autopsy, the patient weighed about 65 pounds. There was extensive caseocavitary tuberculosis in the remaining right lung with a large cavity communicating with the right pleural space. A 1 cm. defect in the esophagus a few centimeters below the main bronchus opened into the left pleural cavity. Microscopically, ulceration and granulation tissue formation were noted. An incidental finding of a liposarcoma of the right frontal lobe of the brain was noted.

CASE 3.—R. L., a 44-year-old white man, was admitted to the VA Hospital, Oteen, North Carolina, for the eighth time in 1956, for the treatment of pulmonary tuberculosis. The onset of his disease, in 1948, was characterized by bilateral disease with a large cavity in the right upper lobe, and tuberculous laryngitis. The patient was treated intermittently with antimicrobial drugs (streptomycin, para-aminosalicylic acid, isoniazid) but treatment was repeatedly interrupted by irregular discharges. Finally in 1955, a right upper lobectomy and resection of the superior segment of the right lower lobe were done. This was followed 20 days later by a six-rib thoracoplasty for a residual apical space. The patient again left the hospital against advice, and was admitted a year later with a pulmonary hemorrhage. Bronchoscopy showed the presence of a bronchopleural fistula of the stump of the superior segment of the right lower lobe. Because of continuing streaking and atelectasis of the basal segments of the right lower lobe, the remainder of the right lung was resected on July 31, 1956. At this time sputum was negative for acid-fast bacilli.

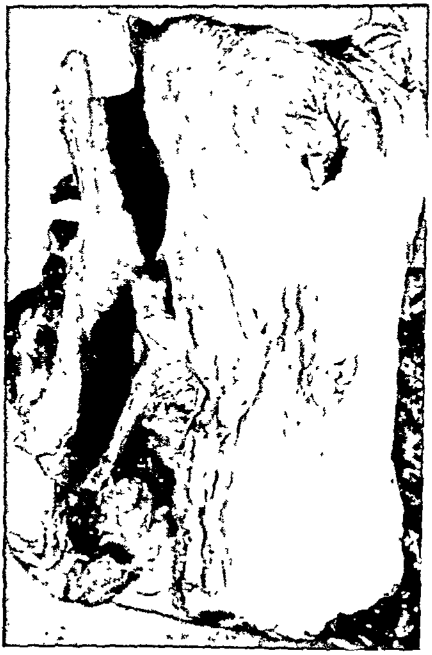

Fig. 4.—Case 3. Autopsy specimen of mid-esophagus (opened) and tracheal bifurcation. A probe is visible in the wide esophageal end of the esophagopleural fistula several centimeters proximal to the level of the carina. This patient died 2½ years after diagnosis of the fistula.

During the course of the operation, which was difficult because of dense adhesions and the presence of a localized empyema in the superior part of the pleural cavity, according to the surgeon's note, ". . . the esophagus was inadvertently mobilized in its middle third, and the azygos vein was severed."

The postoperative course was febrile. On the eighth day after operation, as the sutures were removed, there was purulent drainage from the wound, and an empyema was drained the next day, at first by tube, then by open thoracotomy. Cultures of the empyema contents were negative for acid-fast bacilli, and there was never any clear-cut evidence of a bronchopleural fistula.

Drainage continued for some months. Exactly 5 months after the final resection, coffee which the patient had drunk was noted on the open thoracotomy drainage. The diagnosis of esophagopleuro-cutaneous fistula was made and confirmed by Lipiodol swallow. It was not identified, however, at esophagoscopy. A feeding tube was inserted into the stomach.

The fistula continued to drain small amounts of food and fluid for the next 2½ years, in spite of all attempts to obliterate the empyema space on the right side with Schede thoracoplasty and multiple revision operations. The patient was able to maintain his nutrition fairly well–eating normally without a feeding tube–the weight level being about 20 pounds below the pre-pneumonectomy level.

On Aug. 6, 1959, a final stage of modified Schede thoracoplasty was carried out to unroof completely the infected space. The postoperative course seemed uncomplicated except for moderate serosanguineous drainage from the wound. However, on the fifth postoperative day, 4 hours after a routine change of dressings, the patient was found dead in bed.

Autopsy did not reveal any adequate cause of death. There was a fistulous opening from the esophagus, approximately 3 cm above the level of the carina and about 1 cm. in diameter, into the empty right pleural space (Fig. 4). There was no evidence of bronchopleural fistula. Section through the fistula showed destruction of the esophageal wall with eversion of the mucosa toward the pleura. There was an esophageal gland near the area where the epithelium disappeared, joining inflamed pleura covered by a thick zone of mature granulation tissue.

CASE 4.—D. J. B., a 29-year-old Negro veteran, was admitted to the VA Hospital, Oteen, North Carolina, in 1954 for the treatment of pulmonary tuberculosis. The onset of his disease was in 1953, with cavitary disease of the right upper lung field. A 2-stage Lucite ball plombage thoracoplasty was carried out in November, 1954, with removal of the balls and 7 ribs on the right at the second stage. Because sputum remained positive for acid-fast bacilli and the cavity under the thoracoplasty persisted (shown by roentgenograms), resection of the right upper lobe and a portion of the superior segment of the right lower lobe was performed in April, 1955. A persistently infected subscapular space, with no evidence of bronchopleural fistula or empyema, was treated by a revision thoracoplasty in December of the same year. A suture granuloma of the right upper lobe stump was believed at first to be the source of the continuing positive sputum and hemoptysis. Following cauterization at bronchoscopy, the granuloma was observed to heal but sputum remained positive. Completion of the pneumonectomy was done on Feb. 5, 1957, and except for dense adhesions throughout the right pleural cavity, requiring sharp dissection, there were no unusual problems.

Following this operation, the patient ran a low-grade febrile course. Repeated attempts at pleural aspiration yielded no fluid. Three months later there was an episode of marked elevation of temperature and a roentgenogram showed an air-fluid level in the right pleural cavity. A closed thoracotomy with tube drainage yielded air and pus. The next day grape juice was noted in the drainage, and the diagnosis of esophagopleural fistula was made. It was verified by barium swallow and was noted to be at the level of the seventh to the eighth dorsal vertebrae. Tube feedings were begun and, 2 days after discovery of the fistula, an open thoracotomy was carried out. Nutrition was poorly maintained at first, with weight loss down to 80 pounds, and episodes of acute vascular collapse occurred which required parenteral cortisone therapy. Gradually the patient improved and over the next 2-year period the empyema space was obliterated by modified Schede procedures, exposing the fistulous opening with its firm, rounded edges (Fig. 5). In April, 1959, plastic closure of the esophageal fistulous opening which now measured about 1 cm. in diameter was attempted but without success. A small esophagopleural fistula remains but the patient's nutrition has returned to much more nearly normal levels, his weight ranging up to 115 to 120 pounds.

DISCUSSION

There appears to be little doubt that in the 16 patients of the collected series, in whom the complication was recognized relatively promptly after operation, the esophagopleural fistulas were the result of surgical trauma, sometimes recognized, but usually not. It is a fact that in a difficult technical procedure, even when the possibility of esophageal injury is constantly borne in mind and the esophagus is carefully identified, injury and fistula formation may result.[4] The esophagus is often drawn to the side of maximal disease by contraction of fibrous adhesions or by lymphadenopathy. Occasionally this occurs in a sharply localized area. The degree and site of esophageal deviation can sometimes be identified with accuracy by a barium swallow prior to surgery (Fig. 6). The presence of an unsuspected esophageal diverticulum may also be noted by this means (Fig. 7). The examination of an esophagogram prior to an anticipated difficult pulmonary resection, especially a pleuropneumonectomy or a completion pneumonectomy, appears to be a wise precautionary measure. However, a normal esophagogram may give no clue to the presence of adhesions involving the esophagus, traction upon which may result in tenting of the esophageal wall and inadvertent injury to it during a difficult dissection. This resembles the mechanism more familiar to general surgeons doing gall bladder surgery, by which the common bile duct is tented up and inadvertently injured due to excessive traction on the cystic duct. Sauerbruch reports perhaps the earliest case of this type which involved a traction diverticulum.[5]

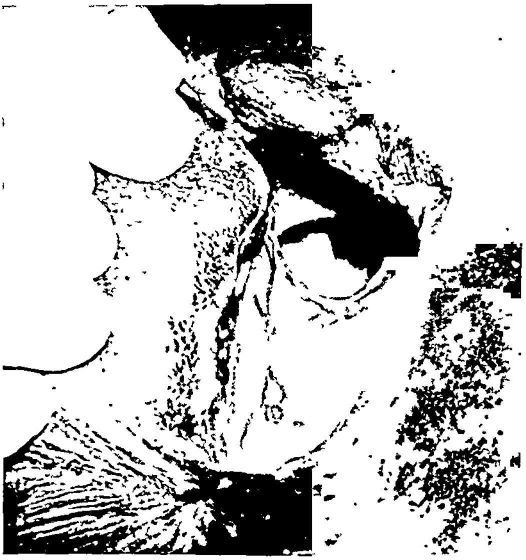

Fig. 5.—Case 4. Gross appearance of defect in esophageal wall communicating widely with small pleural pocket 6 months after diagnosis of esophagopleural fistula was made. The plastic feeding tube in esophagus is visible. This patient retains small fistula 2 years later.

The probability that surgical trauma was involved is much more remote, however, in the remaining 17 patients, in whom symptoms and signs of a fistula appeared for the first time from 3 months to 6 years after operation. In these, some other cause must be sought.

In an attempt to arrive at a more adequate explanation for these late appearing fistulas, two other groups of patients were also studied. One group consisted of 33 tuberculous patients in whom an extrapleural-esophageal fistula developed following an extrapleural surgical procedure, such as extrapleural pneumonolysis, thoracoplasty, etc.[6-18] These were all in adults, most occurred on the right side, and most occurred in association with long-standing infection of the extrapleural space. The French medical literature was the richest source for these case reports, most of them being reported in the past 10 years. The approximate distribution of 27 of these fistulas is noted in Fig. 1, and data regarding them are summarized in Tables II and III. For convenience, these fistulas have been called Type II fistulas, to distinguish them from the first group, or those which followed largely intrapleural surgical operations.

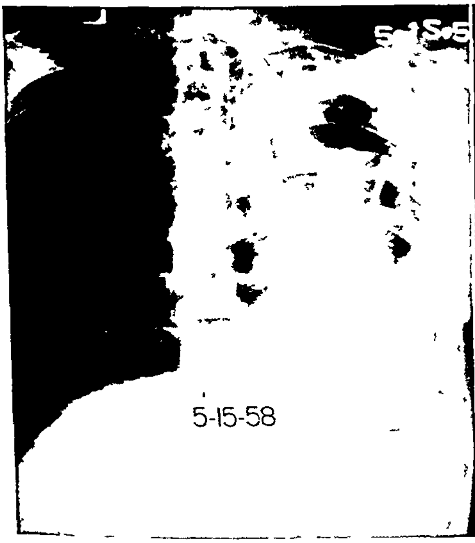

Fig 6.

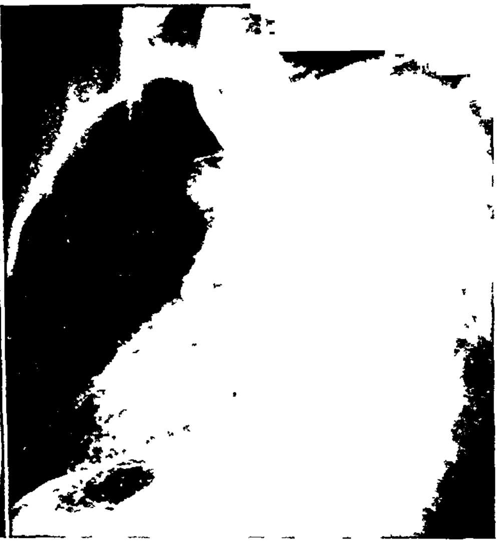

Fig 7.

Fig 6—Unsuspected localized esophageal deviation toward area of chronic tuberculous isease in left upper lung field which was discovered by preoperative barium swallow. Patient ater underwent a left pneumonectomy without complications

Fig. 7—Right anterior oblique view of traction diverticulum of mid-esophagus disovered 2 years after right pneumonectomy for bronchiectasis This patient remains well years following the resection

Last, we were able to collect reports of 35 patients in whom an esophagopleural fistula was discovered associated with and apparently resulting from an intrapleural empyema, often of long duration (up to 14 years!).[19-51] Perhaps these might be more properly labeled pleuroesophageal fistulas. The majority were reported before the era of antibiotics, and largely in association with nontuberculous empyemas. In general, these patients were of a much younger age group (more than half were under 20 years of age). The approximate site of esophageal perforation in 25 of these cases is indicated in Fig. 1. For convenience, we are calling these Type III fistulas (Tables II and III).

The common denominator in most late-occurring Type I fistulas, and in Type II and Type III fistulas was the presence of a pre-existing empyema, often of long duration. It was thought by many observers that these chronic pleural, extrapleural, or mediastinal empyemas, inadequately drained, were responsible for most fistulas not due to direct surgical trauma.

Fistula formation was believed to have occurred in many of all three types of cases as an empyema necessitatis, with rupture into the esophagus. Other significant possibilities mentioned were rupture into the pleural or extrapleural space of suppurating or caseating lymph nodes which had previously established communication with the esophageal lumen; or spread of pleuropulmonary disease (often tuberculosis) by contiguity; or rupture of a traction diverticulum of the mid-esophagus. Erosion of the esophagus by a hard drainage tube was also suggested.

Any of these mechanisms would help to explain the late appearance of some fistulas following the onset of pleural (or extrapleural) infection, and there is certain indirect evidence available to support each postulate.

The preponderance of fistula formation involving the right pleural cavity (75 per cent of the total number of all three types for which data were available) is explainable in part by the anatomy of the esophagus. On the right side, this organ is intimately associated with the mediastinal pleura, while on the left side it is separated from the pleura by the aorta through much of its course. Following extrapleural dissections, this organ would therefore be even more vulnerable on the right side to injury or infection or both, than it would on the left.

The occurrence of intense mediastinal lymphadenopathy in and about the carinal and subcarinal areas might also help to explain the localization of many fistulas at the mid-esophageal level. This is the level at which perforation of the esophagus by tuberculous lymph nodes has most commonly been noted,[52] and also at which bronchoesophageal and tracheoesophageal fistulas, as well as traction diverticula, most often occur.[53-58] The causative pathologic changes in the "middle lobe syndrome" are also located at this level. There are interesting case reports in which various combinations of these conditions, such as the "middle lobe syndrome," broncholithiasis, traction diverticula, and esophagorespiratory fistulas, have occurred in the same patient,[59-62] apparently linking them in a pathogenetic chain of events which may include, in some cases, the development of esophagopleural fistulas.

While there are isolated autopsy findings implicating caseous lymphadenopathy (Arandes Adan[6]) and traction diverticulas (McCormick,[37] Crawford[23] and possibly our Case 3) in the development of esophagopleural fistulas, in most cases pathologic data are so meager, and distortion of structures by longstanding infection and extensive fibrosis is so thorough, that the true pathogenesis of many chronic esophagopleural fistulas remains obscure.

The treatment of esophagopleural fistulas of whatever cause is complicated and unsatisfactory. Nevertheless, every attempt should be made to maintain nutrition, eliminate infection, obliterate empyema spaces, and restore function if possible. Extensive esophageal reconstructive procedures such as bowel transplants proved to be fatal in every case of Type I fistula. Haight's* patient, with a Type II fistula (following a thoracoplasty), recovered after colon transplant, a healing empyema drainage tract remaining. In most cases, more conservative operations on the chest wall (Schede thoracoplasty, muscle flap) or on the mediastinum or esophagus (direct closure, or excision and re-anastomosis of the esophagus), while often not curative, were at least considerably safer. Jejunostomy for the maintenance of nutrition was much more satisfactory than gastrostomy, or even tube feedings, because regurgitation of stomach contents through the fistula was thereby avoided. In those patients in whom no definitive surgical therapy (other than gastrostomy or jejunostomy) was done or was possible, the mortality rate was 90 per cent.

SUMMARY AND CONCLUSIONS

Esophagopleural fistula is an uncommon but not rare complication of thoracic surgery, especially of the surgery of pulmonary tuberculosis. Four cases were observed in 934 pulmonary resections for tuberculosis. Twenty-nine additional cases following intrapleural procedures were contributed for this study by surgeons in many parts of the United States and India and these were compared with 33 cases of esophagopleural fistulas following extrapleural thoracic surgical procedures, such as thoracoplasty and extrapleural pneumonolysis. In addition, a group of 35 cases of benign esophagopleural fistulas following empyema, not associated with a prior thoracic surgical procedure, was also analyzed.

Fistulas which appeared soon after operation (within 3 months) were thought to be due most often to surgical trauma, while those which appeared late (from 3 months to 8 years following surgery) were thought to be due to chronic infection. The exact sequence of events by which perforations of the esophagus were brought about was often obscure.

Treatment has been in general unsatisfactory and the mortality and morbidity rates were high. Suggested preventive measures include preoperative esophagograms to detect unusual deflections or unsuspected diverticula of the esophagus, and prompt and vigorous obliteration of postoperative infected spaces. The gravity of this complication is emphasized by the over-all mortality rate of 51 per cent.

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REFERENCES

1. Muller, W. H., Jr., Byron, F. X., and Power, H. W.: Delayed Traumatic Rupture of the Esophagus, J. THORACIC SURG. 25: 371-379, 1953.
2. Pecora, D. V.: Tuberculous Fistula of the Esophagus, J. THORACIC SURG. 36: 53-57, 1958.
3. Stander, L. H., and Robinson, H. H.: Spontaneous Esophageal Cutaneous Fistula, Am. Surgeon 25: 248-251, 1959.
4. Strieder, J. W.: Personal communication, 1959.
5. Sauerbruch, F., and O'Shaughnessy, L.: Thoracic Surgery, London, 1937, Edw. Arnold & Co., pp. 316-319.
6. Arandes Adan, R., and Vilar Bonet, J.: Fistulas esofagopleurales y extrapleurales, Med. clin. 16: 14-17, 1951.
7. Barrie, J., and Poliak, D.: Deux cas de fistule oesophagoextrapleurale, Poumon et coeur 11: 353-355, 1955.
8. Berard, M., and Juttin, P.: Les fistules oesophagopleurales et extrapleurales, Rev. tuberc. 13: 225-231, 1949.
9. Colantuono, P., and Spadoni, G. M.: Empiema extrapleurico con fistula esofagea, Ann. Ist. Carlo Forlanini 10: 97-103, 1947.
10. Dambrin, P., Gourdon, J., Eschapasse, LeBayan P., and Coll, J.: Les complications oesophagiennes du pneumothorax extrapleural, Toulouse méd. 57: 127-137, 1956.
11. Daumet, P., Garnier, C., and Ortega, J.: A propos de deux fistules oesophagoextrapleurales operees, Poumon et coeur 11: 357-359, 1955.
12. Gokce, T. I., and Erbelger: Perforation spontanee de l'oesophage par complication rare du pneumothorax extrapleural, Rev. tuberc. 16: 1023-1026, 1952.
13. Jaccottet, H.: La fistule oesophagoextrapleural, These, Lausanne, 1954.
14. Klarnet-Legendre, R., and Gugelot, A.: Fistule oesophagoextrapleurale dans un double pneumothorax, Rev. tuberc. 13: 648-650, 1949.
15. Lortat-Jacob, J. L., Le Brigand, Hummel, and Triboulet: Trois cas de fistule oesophagienne du pneumothorax extrapleural avec decortication, cure operatoire et guerison de la fistule, Poumon et coeur 11: 361-370, 1955.
16. Paviot, J. J., and Demirleau, J.: Complication mortelle d'un plombage extrafascial a l'aide de sachets de polythene: fistule ocsophago-tracheoextra-fasciale, Poumon, Paris 8: 423-425, 1952.
17. Zimmer, K. D.: Thorakoesophageal Fistel nach extrapleuraler Pneumolyse, Beitr. Klin. Tuberk. 96: 159-170, 1941.
18. Zubiani, M., and Rossi, S.: Su due casi di fistole esofogee tardive in pneumotorace extrapleurico complicato da empiema, Lotta tuberc. 26: 78-88, 1956.
19. Abbott, O. A., Abnormal Esophageal Communications, Their Types, Diagnosis and Therapy, J. THORACIC SURG. 14: 382-392, 1945.
20. Acuna, M., and Bettinotti, S. I.: Fistula esofagica consecutiva a una pleuresia mediastinica, Semana méd. 2: 96-98, 1930.
21. Arquellada, A. M.: Un caso de communicacion de esofago con pleura, Méd. ibera 10: 77-78, 1920.
22. Ballin, M., and Saltzstein, H. C.: Perforation of the Esophagus. Report of a Case of Transpleural Esophageal Fistula, Surg. Gynec. & Obst. 34: 42-50, 1922.
23. Berman, J. K., and Walters, C. E.: Empyema Complicated by Bronchoesophagopleural Fistula, Ann. Surg. 117: 100-105, 1943.
24. Blauvelt, H.: Pleuroesophageal Fistula in Empyema, Brit. J. Surg. 26: 46-53, 1938.
25. Bullough, W. A.: Rupture of Empyema Into Oesophagus, Lancet 2: 1075, 1911.
26. Caubarrere, N. L.: Un tipo de fistula del esofago, An. de Oto-rino-laring. d. Uruguay 4: 77-84, 1934.
27. Cohen, W., and Sindell, E. A.: Esophagopleural Fistulas. A Case Report With a Review of the Literature, West. J. Surg. 50: 238-249, 1942.
28. Crawford, B. L.: Diverticulum of Esophagus Communicating With Right Empyema Cavity, Proc. Path. Soc., Philadelphia 23: 28-29, 1920-1921.
29. Fioretti, G. P.: Fistole pleuroesofagie; studio anatomio-istologico, Arch. tisiol., Napoli 12: 279-289, 1957.
30. Foot, A. W.: Empyema Opening Into Oesophagus, Proc. Path. Soc. Dublin 9: 11-13, 1880-1882.
31. Fonte, C.: Perfuracoes oesophagopleurales, Brasil-med. 36: 4-6, 1922.
32. Hand, A., and Lee, W. E.: Transpleural Esophagocutaneous Fistula, Ann. Surg. 78: 96-99, 1923.
33. Kanter, A. J., and Madoff, I.: Esophagopleural Fistula in a Case of Tuberculous Pyopneumothorax, Am. Rev. Tuberc. 35: 190-197, 1937.
34. LeLourd, R.: Fistule oesophagopleurale chez un tuberculeux pulmonaire, Rev. tuber 9: 270-272, 1944-1945.

35. LeTulle, M.: Sur une complication rare de la pleuresie purulente: la fistule esophago-pleurienne, Semaine méd. Paris 10: 377-378, 1890.
36. Martens, H.: Note on Pleuroesophageal Fistula, Berl. klin. Wchnschr. 40: 876, 1903.
37. McCormick, E. J.: Transpleural Esophagocutaneous Fistula Following Suppuration, Ohio State M. J. 24: 290-291, 1928.
38. Mikula: Perforation de l'oesophage due á une pleuresie purulente, Ann. d'oto-laryng. 8: 492, 1933.
39. Paulino Filho, A., and Olinto, M.: Em torno de um caso de fistula esofago-pleural, Bol. d. inst. clin. quir. 18: 227-237, 1942.
40. Phillips, J. R.: Esophagopleural Fistula; Case, Radiology 32: 91-92, 1939.
41. Samuelson, N.: Ett Fall af Fistula oesophagopleuro-thoracico, Festkrift, Stockholm, 1894, F. W. Warfringe, pp. 227-230.
42. Sayago, G., and Wolaj, I. F.: Perforacion de esofago en el curso de la tuberculosis pulmonar, Semana méd. españ. 1: 861-866, 1940.
43. Sigora, B.: Oesophagusperforation in Verbindung mit Traktionsdivertikel, Roentgenpraxis 2: 140-143, 1930.
44. Sindel, E. A.: Empyema Necessitatis, Quart. Bull., Sea View Hosp. 6: 1-49, 1940.
45. Thursfield, H.: A Case of Pleuroesophageal Fistula, Tr. Path. Soc., London 55: 51-53, 1901-1902.
46. Torbett, J. W., Jr., and Bennett, A. C.: Esophagopleural Fistula: A Complication of Empyema, Am. J. Surg. 52: 129-132, 1941.
47. Valli, M.: Raro caso di fistula pleuroesofagea da empiema tubercolare, Minerva Med. 1: 154-155, 1940.
48. Voelcker, A. F.: A Case of Empyema in Which a Communication Was Established With Esophagus, Tr. Clin. Soc. London 24: 86-90, 1890-1891.
49. Vos, P. A.: Doorbraak Van een Empyeem in den Slokdarm Transthoracale Oesophagusfistel, Nederl. tijdschr. v. geneesk. 2: 1940-1941, 1923.
50. Wall, C. K.: Transthoracic Esophageal Fistula Following Thoracotomy for Empyema, J. M. A. Georgia 21: 71-75, 1932.
51. Young, R. E. S.: Pleuroesophageal Fistula in Empyema, J. THORACIC SURG. 10: 672-674 1941.
52. Frostad, S.: Segmental Atelectasis in Children With Primary Tuberculosis, Am. Rev. Tuberc. 79: 597-605, 1959.
53. Clagett, O. T., Payne, J. H., and Moersch, H. J.: Acquired Esophagotracheobronchial Fistula, Surg. Gynec. & Obst. 82: 87-90, 1946.
54. Coleman, F. P., and Bunch, G. H., Jr.: Acquired Nonmalignant Esophagotracheobronchial Fistula, J. THORACIC SURG. 19: 542-558, 1950.
55. Hughes, F. A., Jr., and Fox, J. R., Jr.: Acquired Nonmalignant Esophagotracheobronchial Fistula—Report of 2 Cases, J. THORACIC SURG. 27: 384-389, 1954.
56. Bevermann, C.: Ein Beitrag Zur Lehre uber Traktionsdivertikel der Speiserohre, Erlangen, 1904, Univ. Buchdr.
57. Capellini, E.: I. Diverticuli dell' esofago toracico, Rass. ital. chir. med. 6: 407, 1957.
58. De Bakey, M. E., Heaney, J. P., and Creech, O.: Surgical Considerations in Diverticula of the Esophagus, J. A. M. A. 150: 1076-1082, 1952.
59. d'Abreu, A. L.: A Practice of Thoracic Surgery, London, 1953, Edward Arnold & Co. p. 456.
60. Jenkinson, D. L., and Bate, L. C.: Esophagobronchial Fistula Through an Esophageal Diverticulum, Am. J. Roentgenol. 66: 236-240, 1951.
61. Katz, H. L.: Traction Diverticula of the Esophagus in Middle Lobe Syndrome, Am. Rev. Tuberc. 65: 455-464, 1952.
62. Kidd, H. M., and Christopherson, E.: Broncholithiasis and Bronchoesophageal Fistula, Canad. M. J. 64: 142-146, 1951.
63. Chalnot, Girard, and Lochard: Fistule oesophagopleurale dans un pneumothorax intrapleural gauche. Guerison par thoracoplastie et plastie musculaire, Rev. méd. Nancy 75: 212-214, 1950.

THE SURGICAL TECHNIQUE FOR THE CORRRECTION OF PECTUS EXCAVATUM

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SINCE the appearance of Brown's paper in 1939[1] on the surgical treatment of pectus excavatum, or funnel chest, thoracic surgeons have shown a lively interest in this deformity.

It is now generally accepted that, when surgical correction is indicated, some type of the so-called radical operation is indicated. Various writers have outlined a number of techniques for this operation and, in general, they differ little.[2-6] These differences have principally been concerned with the method of external maintenance of the refashioned chest wall. While external struts or ladders, or internal fixation by pinning were almost universally performed a few years ago, the trend has been to modify or discard their use.[7]

We should like to present our technique which is a further modification and, we believe, a significant improvement for two reasons. In the first place, the one universally accepted indication for operative correction of funnel chest is the cosmetic one. Our operation is designed to effect a more nearly perfect cosmetic result than those previously described. In the second place, paradoxical movements of the sternum and chest wall are eliminated by solid fixation without the necessity of internal or external struts.

TECHNIQUE

Intratracheal anesthesia is employed with the patient supine on the operating table. In males, a midline sternal incision is employed, whereas in females, a transverse submammary incision is used. The midline incision is easier and gives better exposure but admittedly often results in scars which tend to widen. The skin incision begins at the cephalad end of the depression and is carried downward to a point midway between the xiphoid cartilage and the umbilicus (Fig. 1). Next, the pectoral muscles and their fascia are separated by sharp dissection from the underlying sternum and costal cartilages. This stripping is carried from the midline laterally to slightly beyond the costochondral junctures. The depression invariably begins medial to these junctures.

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The anterior rectus fascia is then divided and the two rectus muscles are separated through the full extent of the skin incision. Care is taken not to enter the peritoneal cavity during this maneuver. The origins of the two rectus muscles are freed from the lower costal margins and xiphoid process, and turned laterally as seen in Fig. 1. The xiphoid process is usually excised to facilitate this maneuver.

At this point, T incisions of the periosteum are made at the costochondral junctures. The periosteum is stripped with a small periosteal elevator to expose the most lateral 2 cm. of the costal cartilages. These exposed 2 cm. of cartilage are resected and discarded. The resections are begun at the lower costochondral junctions and are carried upward to the level of the beginning of the sternal depression which usually includes the third costochondral junction.

By blunt dissection with a peanut dissector, the diaphragm is freed from the posterior wall of the body of the sternum. We have been impressed that very little fibrous connection is found between the xiphoid-sternum and the diaphragm. Next, the intercostal bundles are divided between the resected cartilages so that the entire breast plate is attached above only through the body of the sternum. The anterior plate of the sternum is then divided transversely with an osteotome just above the level where the sternal depression begins. This is usually at the third intercostal space. The entire freed breast plate is elevated until the posterior plate of the body of the sternum is cracked. The freed breast plate then resembles a pair of wings (Fig. 2) with a central depression.

The freed sternum and attached portions of cartilages and intercostal muscles are fashioned to produce a perfectly flat contour by multiple cuts. These cuts are made transversely through the costal cartilages in as many places as necessary to remove all depressions. Since the sternum itself almost invariably has a central depression, it must also be flattened to effect a perfect cosmetic result. This is accomplished by multiple longitudinal and transverse sectionings of its anterior plate, after which the posterior plate is broken by hyperflexion of the sternum. The number of these transections of both the sternum and the costal cartilages varies in each case, depending upon the severity of the deformity and the age of the patient. In a child the sternum can be cut with an osteotome. In adolescent and adult patients we use an electric Stryker saw to cut the sternum. The costal cartilages can always be cut with a knife. Fig. 2, *a* shows the costal cartilages being cut. After these multiple cuts, the sternum and attached costal cartilages have the appearance of diced bone and cartilage held together by fibrous tissue and intercostal muscle.

After the sternal plate has been flattened, it occupies a wider area than the space from which it came. The excess cartilage and intercostal tissue is excised with a scissors so that the free plate will fit into the created defect. In Fig. 2, *a* the areas lateral to the dotted lines represent the portions of cartilage and intercostal tissue to be excised and discarded. We cannot overstress the importance of being careful to eliminate all sternal and costal depressions, as this is the secret of a good cosmetic result.

The flattened, trimmed, diced plate is fitted back into its space, but it will now be noted that it rides higher and that the costal cartilages do not necessarily meet with their previous costal counterparts (Fig. 3). Several of the lower ribs will not have any cartilages adjoining them.

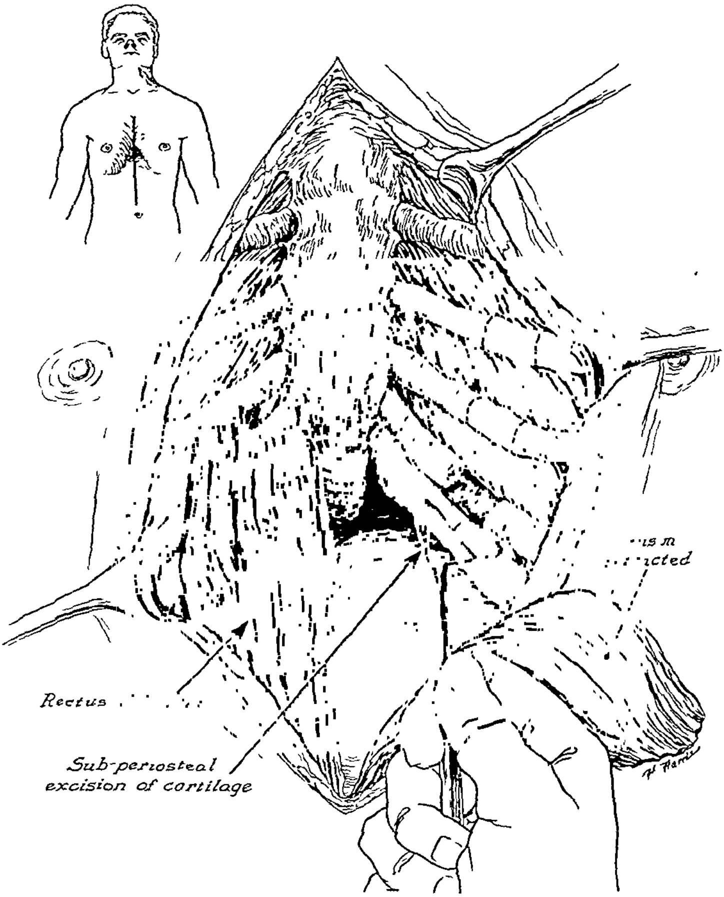


Fig. 1.—The reflection of the freed recti muscles is shown, as well as the resection of segments of cartilage, at the costochondral junctions. Inset shows the extent of the skin incision.

The plate is anchored firmly in place by interrupted sutures between intercostal muscles and costal cartilages. These sutures vary in number depending on whatever seems to be necessary to produce a completely stable chest wall. As shown in Fig. 3, *a*, several stabilizing sutures are also taken in the transected sternum at its top.

The rectus muscles are brought together in the midline by interrupted sutures through the anterior rectus fascia. The rectus muscles are not attached to the costal margin in order to avoid drawing the sternum down again. A defect then remains between the approximated rectus muscles and the xiphoid area. This defect causes no later herniation as it is supported posteriorly by

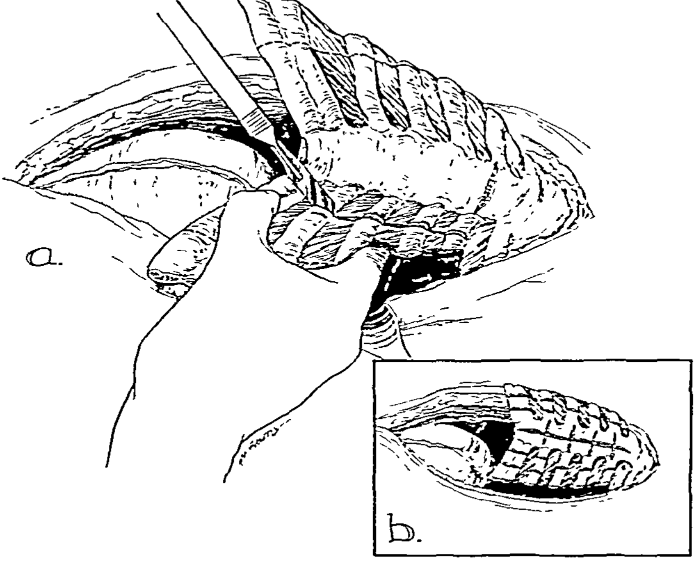


Fig. 2.—*a*, Note the winged appearance of the freed sternum and attached costal cartilages. The beginning of multiple transections of the cartilages is shown. The dotted lines indicate the portions of cartilage and intercostal muscle to be excised.

b, The appearance of the breast plate after multiple cuts of the sternum and cartilages have been made. The excess cartilage has also been excised.

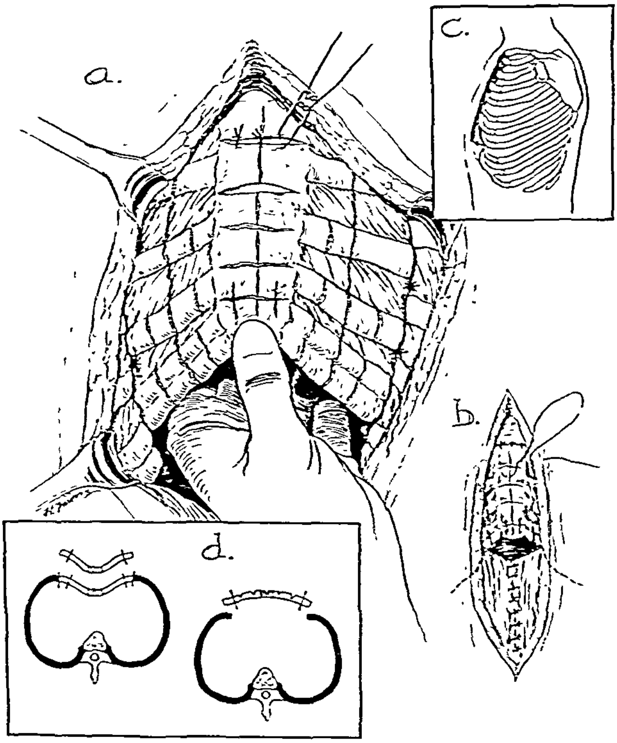
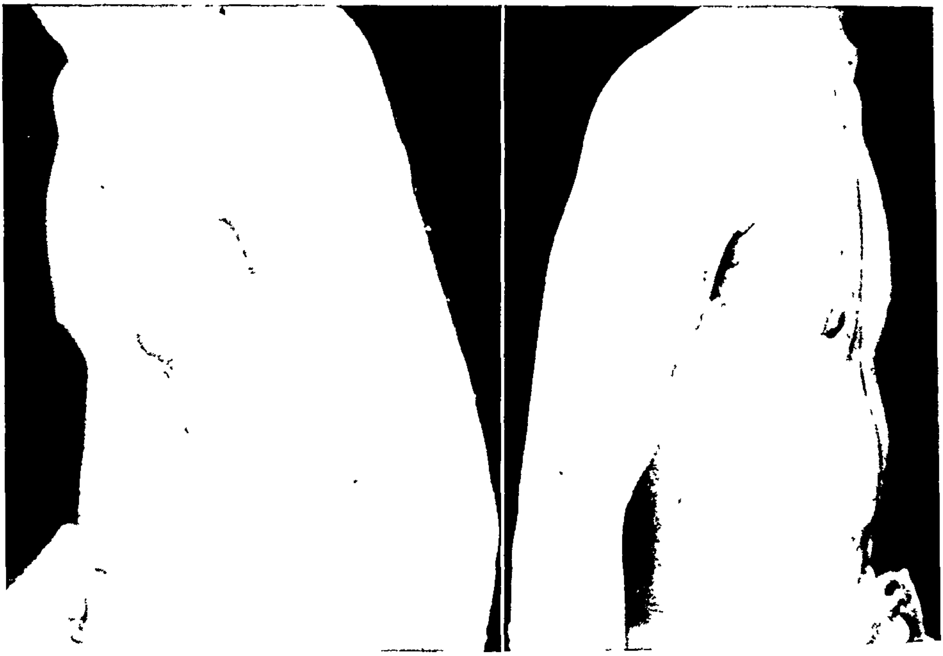


Fig. 3.—*a*, The refashioned breast plate is shown fixed in its new position by interrupted sutures. Note that the costal cartilages now do not necessarily meet the ribs.

b, The rectus fascia has been joined in the midline by interrupted sutures. The first suture joining the pectoral fascia is being inserted and is shown passing through the periosteum of the body of the sternum.

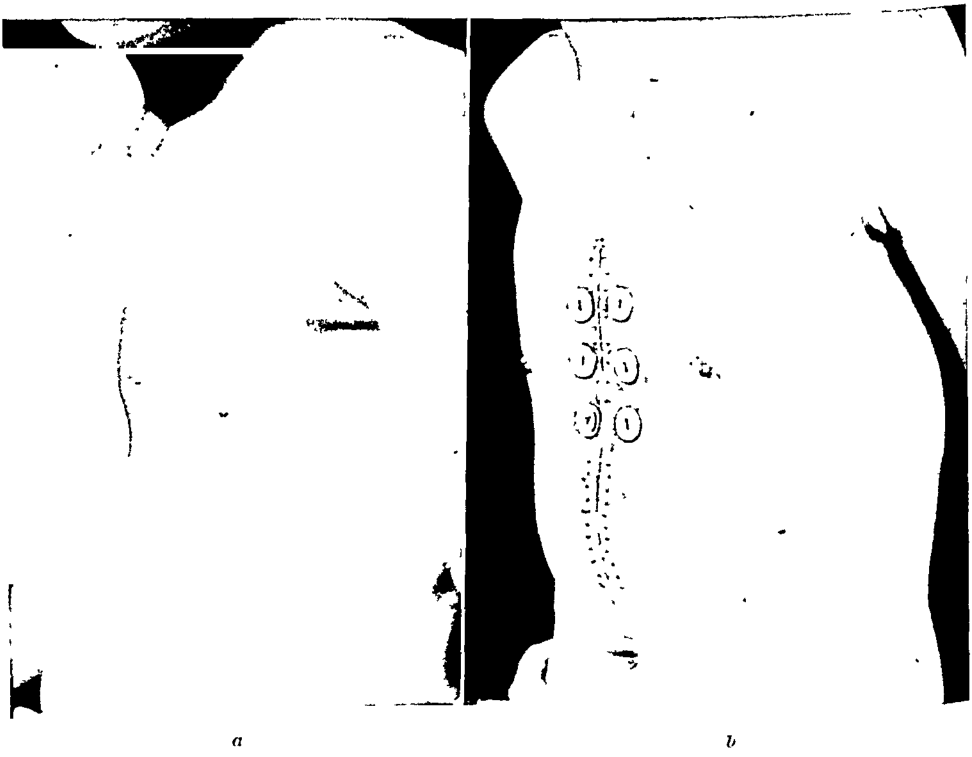
c, A lateral view showing the new position of the sternum.

d, Horizontal body section showing the method of overcorrection of the breast plate by multiple transections and final trimming.



a. *b.*

Fig. 4.—*a*, The appearance of a 17-year-old boy before operation for funnel chest. *b*, The appearance of the same patient after operation for funnel chest.



a *b*

Fig. 5.—*a*, The appearance of a 15-year-old boy before operation for funnel chest. *b*, The appearance of the same patient after operation for funnel chest showing retention sutures over buttons still in place.

the diaphragm. The pectoral fascia is brought together by interrupted sutures, taking a bite also in the midline periosteum of the body of the sternum with each suture (Fig. 3, *b*).

In dividing the intercostal muscles, the pleura is usually entered on at least one side and often on both sides. If a small pleural hole is produced, it is closed. But a large opening is always left in one pleural cavity so that the retrosternal drainage can run into this pleural cavity. A chest tube, connected to an underwater-seal, is brought out of this chest cavity through a separate stab wound lateral to the breast.

The skin is reapproximated with interrupted sutures. When a midline incision is employed, three or four wire-retention sutures are placed in the skin tied over buttons in an effort to prevent tension and subsequent widening of the scar.

The chest tube is removed the next day. The patient is usually allowed out of bed in several days. Children appear to tolerate the pain of the procedure better than adults. The patient is discharged home between the eighth and tenth postoperative day. The wire-retention sutures are removed in 2 weeks. Strenuous activity is restricted for several months. Figs. 4 and 5 demonstrate the results obtained using the described method on two adolescent patients.

SUMMARY

A modified technique for the radical repair of pectus excavatum is presented. We feel that this technique effects a more nearly perfect cosmetic result than previously described methods. In addition, it offers greater stability of the chest wall without the necessity of internal or external struts.

REFERENCES

1. Brown, A. L.: Pectus Excavatum (Funnel Chest), J. THORACIC SURG. 9: 164, 1939.
2. Lester, C.: Surgical Treatment of Funnel Chest, Ann. Surg. 123: 1003, 1946.
3. Lester, C.: Funnel Chest: Its Cause, Effects, and Treatment, J. Pediat. 34: 224, 1950.
4. Sweet, R. H.: Pectus Excavatum, Ann. Surg. 119: 922, 1944.
5. Ravitch, M. M.: Operative Treatment of Pectus Excavatum, Ann. Surg. 129: 429, 1949.
6. Lindskog, G. F., and Felton, W. L.: Considerations in the Surgical Treatment of Pectus Excavatum, Ann. Surg. 142: 654, 1955.
7. Mahoney, E. B., and Emerson, G. L.: Surgical Treatment of the Congenital Funnel Chest Deformity, A. M. A. Arch. Surg. 67: 317, 1953.
8. Welch, K. J.: Satisfactory Surgical Correction of Pectus Excavatum Deformity in Childhood, J. THORACIC SURG. 36: 697, 1958.
9. Adkins, P. C., and Gwathmey, O.: Pectus Excavatum: An Appraisal of Surgical Treatment, J. THORACIC SURG. 36: 714, 1958.

MYOCARDIAL NECROSIS FOLLOWING ELECTIVE CARDIAC ARREST INDUCED WITH POTASSIUM CITRATE

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ELECTIVE cardiac arrest, induced in the course of open cardiac operations with cardiopulmonary bypass, has been found to be a valuable technical adjunct. In particular, the quiet and dry field it provides greatly facilitates the repair of the more complex anomalies. Of the various methods available for producing elective asystole, the technique devised by Melrose[1] has been most widely employed. In this technique, the heart is arrested by the injection of a solution of potassium citrate into the ascending aorta, proximal to an occluding clamp. This method of arrest was often employed at the National Heart Institute and its advantages seemed clear. Sometimes, however, difficulty was encountered in re-establishing effective myocardial contraction and an occasional patient presented clear evidence of left ventricular failure in the post-arrest period. These observations suggested a physiologic evaluation of the effects of potassium citrate on myocardial function.[2] The hearts of 2 patients who died after potassium citrate arrest revealed, on routine histopathologic study, unusual areas of necrosis and prompted a detailed pathologic re-examination of the hearts of all patients who died following open cardiac operations. The results of these studies in 30 patients are described in the present report.

MATERIALS AND METHODS

Material available for the study consisted of the hearts of 30 patients who had died at various intervals following direct vision intracardiac operations. Nineteen patients had had elective cardiac arrest induced with potassium citrate. In none of the remaining 11 patients had this technique been employed; in 9 no form of arrest was used and arrest was induced in 2 by aortic occlusion alone. In every patient, total cardiopulmonary bypass was provided by either a modified Melrose pump-oxygenator (12 patients) or a rotating disc oxygenator with a nonocclusive roller pump (18 patients). Systemic flow was, in general, provided at a rate of 2 L. per minute per square meter of body surface area and the duration of perfusion varied from 9 to 113 minutes.

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When elective arrest with potassium citrate was induced, a solution of 2.5 per cent potassium citrate was prepared by diluting a 25 per cent solution with nine volumes of fresh, heparinized blood. The aorta was cross-clamped immediately distal to the heart and the arresting solution was injected as rapidly as possible into the aortic segment until complete myocardial paralysis was observed. Following completion of the intracardiac procedure, coronary flow was restored by removal of the aortic clamp. In all instances the right heart was drained during the recovery period to prevent distention. The periods of aortic occlusion ranged from 6 to 67 minutes.

Routine pathologic examination of the hearts of these 30 patients had been made at the time of autopsy and they had been fixed in formalin and stored. They were re-examined grossly and full-thickness sections were prepared from blocks taken from the anterior wall, posterior wall, and apex of the left ventricle as well as from the ventricular septum and the wall of the right ventricle. Additional sections of both coronary arteries were also studied. Although these various sections were taken from pre-determined places in the ventricles, care was taken to avoid the surgical incisions or other obviously traumatized areas.

RESULTS

A distinctive type of necrosis was observed in various portions of the myocardium in the hearts of 15 (79 per cent) of the 19 patients subjected to potassium citrate arrest. The distribution and severity of the necrotic myocardial lesions, together with pertinent clinical data, are presented in Table I. This lesion was not observed in any of the hearts of the 11 patients who did not receive potassium citrate at the time of intracardiac surgery.

Characteristically the lesions consisted of multiple, sharply circumscribed, microscopic areas of necrosis which usually occurred in the central portion of the ventricular myocardium. Their appearance is shown, at various magnifications, in the representative photomicrographs reproduced in Figs. 1 through 5. The necrotic fibers were swollen and stained intensely with eosin. The cytoplasm in these fibers was either hyalinized or granular and neither cross striations nor longitudinal fibrils could be seen. The nuclei were large and stained strongly with hematoxylin. Even in the acute lesions, those observed in patients who died 2 hours or less after cardiac arrest, there was already disintegration and dissolution of portions of the necrotic fibers and granular debris could be seen between the larger, intensely stained fragments. A striking feature of the lesions was the absence of both hemorrhage and congestion. The cut surface of the myocardium in those hearts exhibiting the largest and most diffuse lesions was grossly dark and discolored. This darkened, mottled appearance was more pronounced in the central portions of the myocardium and often the subendocardial zone was quite pale. The over-all appearance followed closely the distribution of the lesions as shown in Figs. 1 and 2.

The amount of myocardial necrosis varied from single isolated microscopic areas observed in one histologic section, to massive necrosis, involving as much

TABLE I. CLINICAL SUMMARIES AND PATHOLOGIC FINDINGS IN PATIENTS SUBJECTED TO CARDIAC ARREST WITH POTASSIUM CITRATE

PATIENT AND NUMBER	AGE (YR.)	SEX	DIAGNOSIS	DURATION OF CARDIO-PULMONARY BYPASS (MIN.)	DURATION OF ARREST (MIN.)	VOLUME OF 2.5% K CITRATE (C.C.)	DURATION OF LIFE AFTER ARREST	DEGREE AND DISTRIBUTION OF MYOCARDIAL NECROSIS*			
								LVA	LVP	SEPTUM	RV
1. E. R. (01-59-24)	1½	M	Ventricular septal defect	20	10	50	4 hr.	0	0	0	+
2. D. Y. (01-62-55)	25	F	Ventricular septal defect	34	25	40	5 da.	0	++	+	0
3. P. L. (01-53-77)	5	F	Atrial septal defect and ventricular septal defect	43	22	20	2 hr.	++	0	+	0
4. J. P. (01-74-95)	13	F	A-V canal	28	20	40	26 da.	0	0	0	0
5. W. G. (01-81-62)	42	M	A-V canal	33	20	60	16 hr.	++	++	+++	+
6. L. M. (01-81-69)		M	Tetralogy of Fallot	75	30	60	None	0	0	+	0
7. N. A. (01-68-78)	6	F	Ventricular septal defect	18	6	60	28 hr.	0	0	0	0
8. H. W. (00-85-09)	22	M	Tetralogy of Fallot	31	24	60	48 hr.	0	0	0	0
9. J. K. (01-91-66)	4	F	Ventricular septal defect	26	15	20	1⅓ hr.	++	0	0	+
10. D. S. (00-80-73)	2	M	Ventricular septal defect	30	15	20	28 hr.	0	0	0	0
11. D. Y. (00-88-77)	4	F	Ventricular septal defect	26	13	20	24 hr.	+	0	0	0
12. M. P. (01-94-08)	6	M	Ventricular septal defect	26	20	60	16 hr.	++++	++++	++++	++
13. S. D. (00-93-72)	39	F	Congenital aortic stenosis	25	15	30	10 da.	++++	++++	++++	+
14. R. I. (00-99-66)	8	M	Ventricular septal defect	36	15	30	2 hr.	++++	++++	++++	0
15. A. W. (00-98-42)	7	M	Tetralogy of Fallot	46	15	?	12 hr.	+	0	+	0
16. E. B. (01-85-33)	18	M	Supravalvular aortic stenosis	113	67	90	None	+++	+++	+++	+
17. D. F. (01-83-98)	10	M	Congenital aortic stenosis	25	12	27	12 hr.	++++	++++	++++	+
18. L. B. (00-95-07)	8	M	Tetralogy of Fallot	59	24	30	16 hr.	0	++	0	++++
19. M. D. (02-25-37)	4	F	Tetralogy of Fallot	41	16	25	28 hr.	0	+++	0	+

*LVA = anterior wall of left ventricle; LVP = posterior wall of left ventricle; RV = right ventricle.

as 50 per cent of the myocardium, seen in several sections. These degrees of necrosis were designated as + to ++++ in the various sections examined and their distribution in the anterior wall of the left ventricle (LVA), posterior wall of left ventricle (LVP), ventricular septum and right ventricle (RV) is shown in Table I. The lesions were severe (+++ to ++++) in 6 patients, moderate (++) in 2 patients and mild (+) in 7 patients. No lesions were found in the hearts of 4 patients. It is evident from the data presented in Table I that the lesions were more severe in the left ventricle than in the right, although only one block from the right ventricle was examined.

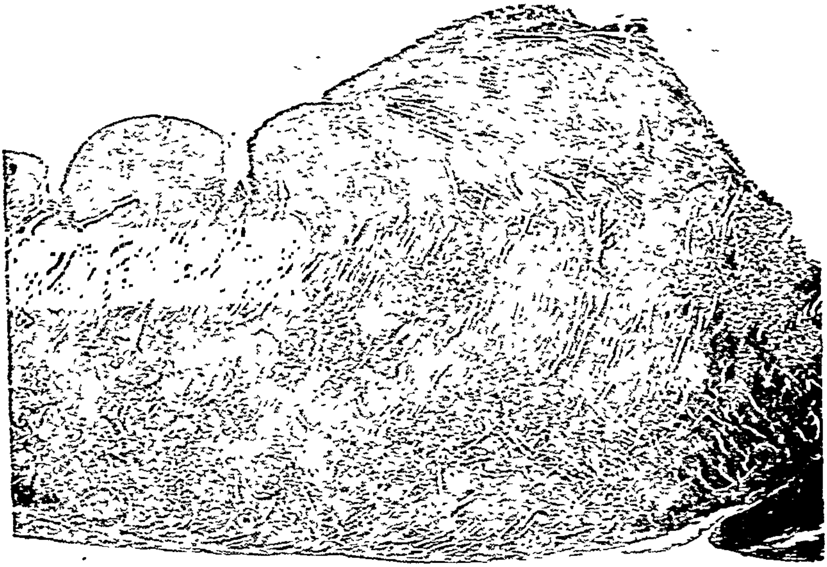


Fig. 1—Patient No 14 (00-99-66) was an 8-year-old boy with ventricular septal defect who died 2 hours after potassium citrate arrest. Multiple, discrete areas of necrosis in the mid-portion of the wall of the left ventricle can be seen. Some of the lesions are confluent. Characteristically these lesions were neither hemorrhagic nor congested. (Hematoxylin and eosin; X8; reduced ½.)

Sections of both the right and left coronary arteries were examined in each heart. The degree of atherosclerosis varied from patient to patient but did not appear to correlate well with either the severity or distribution of the myocardial lesions. Thrombosis or necrosis of coronary arteries was not observed to be associated with any of the lesions. The atria were not examined systematically but a portion of the left atrium was usually included in the block taken from the posterior wall of the left ventricle and necrosis was never observed in it.

In the second group of 11 patients, cardiopulmonary bypass had been employed at the time of intracardiac surgery but cardiac arrest was either not induced (9 patients) or was produced by aortic occlusion alone (2 patients). The anatomic defects necessitating operation and the conditions of perfusion were comparable to the patients listed in Table I. No necrotic myocardial lesions of the type just described were seen in sections of these hearts. Indeed, the only pathologic changes noted were those specifically associated either with the defect for which operation had been performed, with the operative incisions themselves, or the small areas of acute hemorrhage and edema which follow cardiac massage and defibrillation.[3] In most instances, the myocardium appeared normal.

DISCUSSION

The patients are arranged in chronologic order according to the date of operation in Table I. It is apparent that the most severe lesions were encountered in Patients 12 to 19 and less severe lesions were seen in Patients 1 to 11. All 4 of the patients who received potassium citrate but whose hearts did not exhibit necrotic lesions were among the first 11 patients in the table. The date dividing these two groups was May, 1958, and re-examination of the surgical records shows that at this time a change was made in the pharmaceutical preparation of the 25 per cent potassium citrate stock solution. Before this date the solution was prepared in bulk and often had been stored in glass several months before it was used. However, precipitates were noted to form in the solution and flaking of the glass containers was observed. After May,

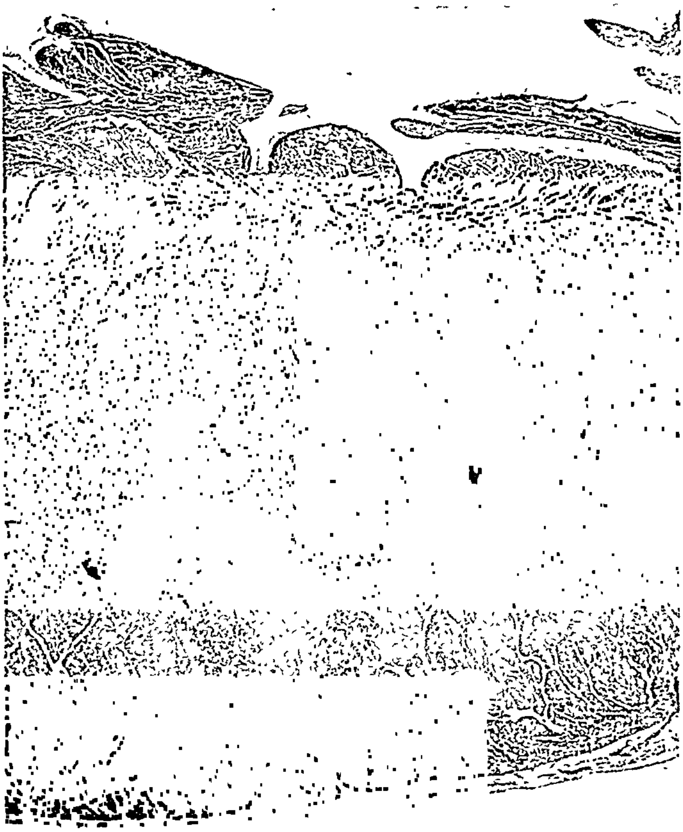


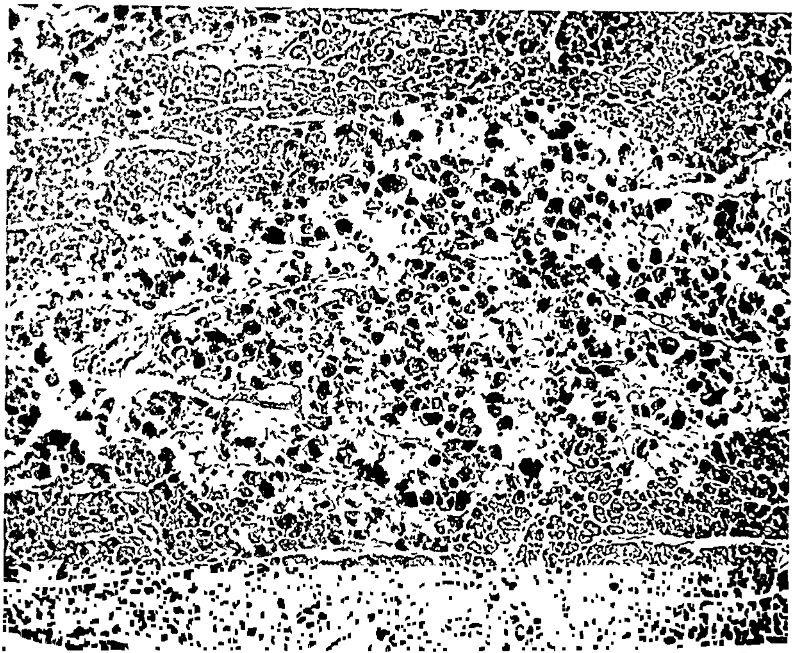
Fig. 2.—Patient No. 17 (01-83-98) was a 10-year-old boy with congenital aortic stenosis who died 12 hours after cardiac arrest with potassium citrate. The massive, confluent areas of necrosis involve more than half of the myocardium of the left ventricle. Note, as in Fig. 1, that the subendocardial and subepicardial layers of the myocardium tend to be spared. (Hematoxylin and eosin; ×100; reduced ⅙.)

1958, the potassium citrate was furnished in crystalline form and the 25 per cent solution was prepared by adding a measured amount of diluent to a weighed quantity of the crystals immediately before use. Following this change in the procedure for the preparation of the potassium citrate solution, every patient who died after potassium arrest had myocardial necrosis. The lesion, in fact, was severe in the hearts of 7 of the 8 patients. It thus seems likely that the drug, when freshly prepared from crystals, resulted in a more toxic solution which was responsible for more severe myocardial damage.

The data presented do not allow a conclusive statement as to the pathogenesis of the myocardial lesions; they were, however, unequivocally associated with perfusion of the heart with potassium citrate. There was no correlation between the occurrence of the myocardial necrosis and the type of congenital defect, the heart size, age, sex, or any other clinical factor that was considered. It is also remarkable that the occurrence and severity of the myocardial lesions do not correlate well with the amount of potassium citrate infused into the coronary arteries. the length of perfusion, or the duration of cardiac arrest. The association of more severe myocardial damage with the change in the preparation of the potassium citrate solution also indicates that the myocardial lesions resulted from its use. Recent experimental work lends further support to this conclusion. Waldhausen and his co-workers[2] showed, in a comparison with acetylcholine and anoxia as arresting agents, that potassium citrate caused severe depression of left ventricular function. Gilbert[4] has demonstrated that the distribution of the potassium citrate solution in the myocardium is by no means uniform and this observation poses the problem as to whether the necrosis occurs in areas which have or have not received the highest concentration of potassium citrate.

After the present study was initiated, Helmsworth and his associates[5] described histologically similar lesions in the hearts of dogs sacrificed 48 hours after cardiac arrest had been induced with potassium citrate. The lesion has also been produced experimentally in the dog in our laboratory and is remarkably similar to the lesions observed in the human being (Fig. 6). This experimentally produced lesion is also remarkable because the profound pathologic changes in the myocardial cells occurred within 30 minutes after perfusion with potassium citrate. Fully developed lesions were also observed within 1 to 2 hours in several of the patients in the study. Older lesions in the patients, lesions observed in patients who died 2 days or longer after operation, exhibited infiltrates of leukocytes and macrophages but were otherwise quite similar histologically to the acute lesions. The myocardial lesions produced by the potassium citrate appear to be distinctive. Study of the fresh lesions in the dog heart suggest that segments of the myocardial fibers have undergone acute disintegration leaving swollen and intensely staining remnants which are widely separated. Capillaries, small arterioles, and connective tissues within the lesion appear to be unaffected. These various features distinguish this lesion from a variety of other types of myocardial necrosis such as occur in acute infarcts,[6] in association with potassium deficiency,[7] or with noradrenalin.[8]

A discussion of the clinical course of patients with widespread myocardial damage of the type described is difficult since in some it was altered or obscured



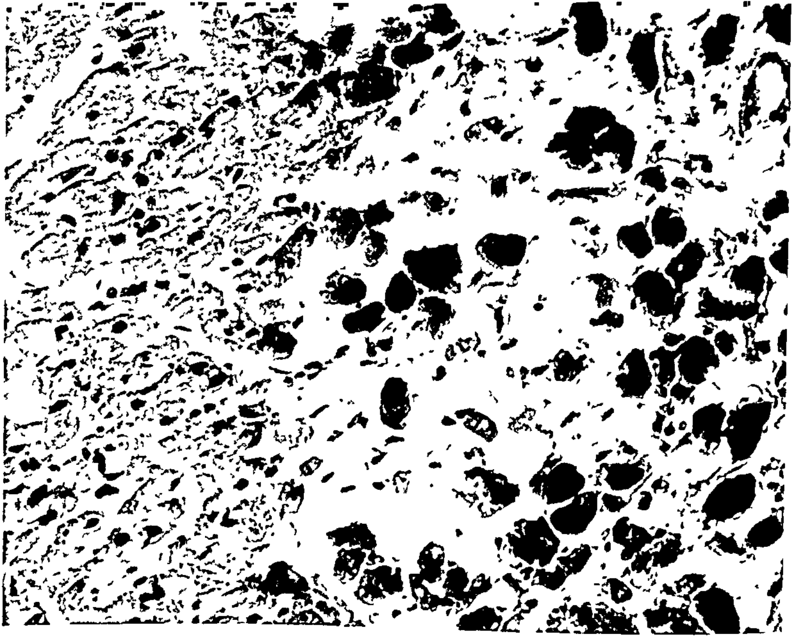


Fig 3.—Same patient as in Figs 1 and 4 This photomicrograph of a single lesion illustrates the discrete, sharp bound[illegible] f necrosis and adjacent, normal myocardium. Many portions of the [illegible] rs have disintegrated and disappeared so that the remaining portions [illegible] appear widely separated. The thin-walled, intramural artery toward one end of the lesion has a normal appearance and its lumen is empty The capillary-sized vessels are prominent because of the altered myocardium but they also appear normal and are free of thrombus The lesion is not hemorrhagic (Hematoxylin and eosin; ×100, reduced ⅓)

Fig 4—Same patient as shown in Figs 1 and 3 The portions of necrotic myocardial fibers which remain in the lesions are enlarged and stained intensely with eosin The cell nuclei are enlarged and stained heavily with hematoxylin Fragments [illegible] tegrated fibers can be seen between the swollen fibers, but many portions of the inj[illegible] have [illegible] out. (Hematoxylin and eosin; ×275; reduced ⅙.)

by other significant factors such as postoperative hemorrhage or an incomplete anatomic repair In others, however, death could clearly be attributed to the left ventricular failure which followed arrest. In these patients gradually

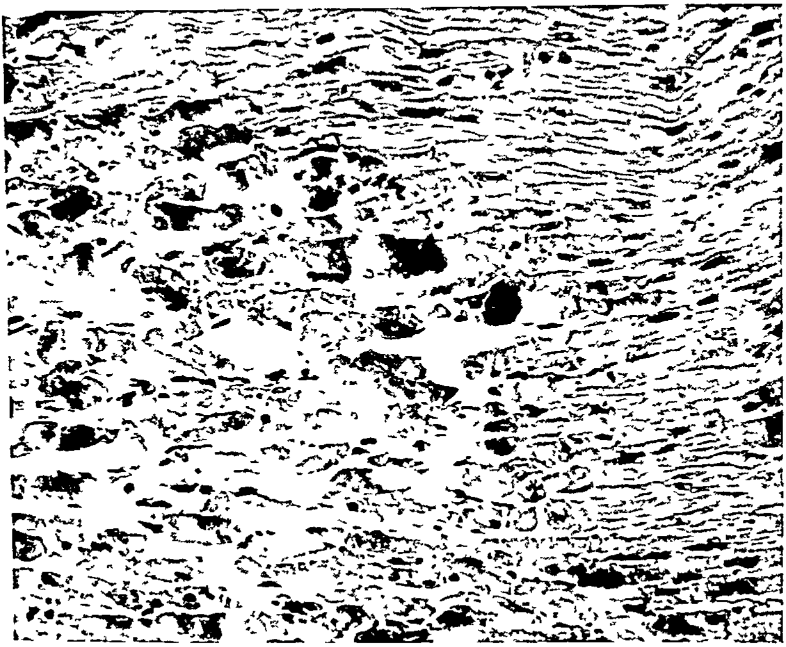


Fig 5.—Patient No 12 ((01-94-08) was a 6-year-old boy who died 16 hours after arrest with potassium citrate and repair of ventricular septal defect The junction between normal appearing myocardial fibers and necrotic fibers is quite sharp Fragmentation and dissolution of portions of necrotic fibers is apparent. (Hematoxylin and eosin, ×275, reduced ⅙)

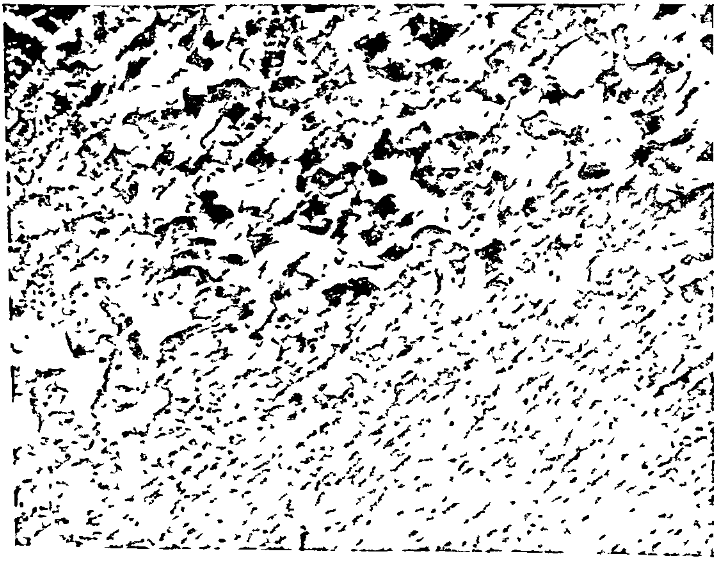


Fig 6.—The histologic appearance of necrotic lesions in the dog heart after cardiac arrest with potassium citrate The lesion is similar to that observed in patients The animal was sacrificed 15 minutes after normal heartbeat was restored (Hematoxylin and eosin; ×100, reduced ⅙)

progressive hypotension was observed which became unresponsive to pressor agents, and was associated with rising venous pressure. One patient (No. 13) apparently survived this acute period of failure, only to die 10 days after operation of an unrelated cause.

The clinical and pathologic observations just described and the experimental demonstration of impaired ventricular function following potassium citrate arrest has led to the abandonment of this technique at the National Heart Institute. Although flaccid paralysis of the heart certainly facilitates the repair of many intracardiac anomalies, the hazard of the method is so great as to outweigh this advantage. A dry and quiet field can be secured by intermittent aortic occlusion alone and this technique is applicable in virtually all procedures in which aortotomy is not necessary. When the aorta must be opened for long periods, as in the repair of aortic valve lesions, direct coronary perfusion has been found the technique of choice.

SUMMARY

Detailed microscopic examinations were made of the hearts of 19 patients who died at various intervals following open cardiac operations in which cardiac arrest had been induced by the infusion of potassium citrate into the coronary bed. In 15 (79 per cent) of the 19 patients, myocardial necrosis of a characteristic type was demonstrated. The lesion was not observed in the hearts of 11 patients who underwent similar procedures without arrest or with arrest produced by aortic occlusion alone. The etiology of the necrosis and its significance in the choice of an operative technique for clinical use is discussed.

ADDENDUM

Since the manuscript was submitted, detailed histologic study of the hearts of 7 additional patients has been made. In 4, anoxic arrest was employed and, in 3, the heart was not arrested. No evidence of myocardial necrosis was found in any section.

REFERENCES

1. Melrose, D. G., Dreyer, B., Bentell, H. H., and Baker, J. B. E.: Elective Cardiac Arrest, Lancet 2: 21-22, 1955.
2. Waldhausen, J. A., Braunwald, N. S., Bloodwell, R. D., Cornell, W. P., and Morrow, A. G.: Left Ventricular Function Following Elective Cardiac Arrest, J. Thoracic Surg. 39: 799, 1960.
3. Kaiser, G. C., Edgcomb, J. H., and Kay, J. H.: Ventricular Fibrillation: An Experimental Study Comparing Various Voltages and Durations of Electric Shock in Defibrillation of the Canine Heart, J. Thoracic Surg. 33: 537-543, 1957.
4. Gilbert, J. W., Jr.: Unpublished observations.
5. Helmsworth, J. A., Kaplan, S., Clark, L. C., Jr., McAdams, A. J., Matthews, E. C., and Edwards, F. K.: Myocardial Injury Associated With Asystole Induced With Potassium Citrate, Ann. Surg. 149: 200-206, 1959.
6. Mallory, G. K., White, P. D., and Salcedo-Salgan, J.: The Speed of Healing of Myocardial Infarction. A Study of the Pathologic Anatomy in 72 Cases, Am. Heart J. 18: 647-671, 1939.
7. Follis, R. H., Jr.: Deficiency Disease, Springfield, Ill., 1958, Charles C Thomas, publisher.
8. Nahas, G. G., Brunson, J. G., King, W. M., and Cavert, H. M.: Functional and Morphologic Changes in Heart Lung Preparations Following Administration of Adrenal Hormones. Am. J. Path. 34: 717-730, 1958.
9. Maling, H. M., and Highman, B.: Exaggerated Ventricular Arrhythmias and Myocardial Fatty Changes After Large Doses of Norepinephrine and Epinephrine in Unanesthetized Dogs, Am. J. Physiol. 194: 590-596, 1958.

DISSECTING ANEURYSM OF THE THORACIC AORTA AS A COMPLICATION OF CATHETER AORTOGRAPHY: SUCCESSFUL SURGICAL TREATMENT

John Y. Templeton, III, M.D., Robert G. Johnson, M. D., and
John R. Griffith, M.D., Philadelphia, Pa.

THE widespread use of translumber aortography which followed the original description of the method by Dos Santos and his colleagues[1] has resulted in numerous reports of complications of the procedure. Recent reviews of these complications have been written by Crawford and his co-workers[2] and McAfee and Willson.[3] In contrast, much less attention has been devoted to the complications of catheter aortography perhaps because this method has been applied much less often.

Abdominal aortography by injection through a catheter introduced by way of the femoral artery was first performed by Farinas.[4] Thoracic aortography by catheterization from the radial artery was described by Radner.[5] This method has been extensively applied with great success in Sweden.[6, 7] The sole complication in a large series of cases was a single mild cerebral injury which occurred following the injection of too high a concentration of opaque substance into the cerebral circulation as a result of incorrect placing of the tip of the catheter. Lane and Peirce[8] reported brachial plexus palsy following extravasation of 70 per cent Diodrast injected through a polythene catheter in an effort to demonstrate an innominate artery aneurysm. Deterling[9] reported the occurrence of cerebral complications presumably resulting from the dislodgment of an atheromatous plaque by a catheter introduced into the aorta from the left ulnar artery.

Dissection of the aorta during the performance of a catheter aortogram has not been reported but the occurrence of this complication with percutaneous translumber aortography is recognized. In an excellent discussion of this problem, Gaylis and Laws[10] presented 2 cases of their own with photographs demonstrating dissection of the abdominal aorta and discussed 5 cases in the literature which they considered similar. More recently, Fineberg and associates[11] reported the occurrence of gangrene of the large intestine and ovaries due to dissection of the abdominal aorta after translumber aortography. This

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complication of translumber aortography results when all or a portion of the bevel of the needle lies in the wall of the aorta so that the opaque material is injected either entirely or in part into the aortic wall.

The purpose of this paper is to report the occurrence of a dissecting aneurysm of the thoracic aorta as a complication of catheter aortography and its successful treatment by excision and replacement with a Dacron prosthesis.*

CASE REPORT

The patient, a 60 year old salesman, was admitted to Jefferson Medical College Hospital on Nov. 18, 1958. He had consulted his local physician because of epigastric distress and a pulsating mass had been found in the upper abdomen. Roentgenograms had confirmed the presence of an abdominal aortic aneurysm and demonstrated an active duodenal ulcer. Except for the complaints associated with the duodenal ulcer, the patient's general condition had been satisfactory, although the electrocardiograms had shown evidence of arteriosclerotic cardiovascular disease.

Physical examination was not remarkable except for the presence of the pulsating epigastric mass. The location of the aneurysm, both on physical examination and on the scout films of the abdomen, raised the question as to whether or not it arose far enough proximally to involve the renal arteries. For this reason a catheter aortogram was performed on Nov. 21, 1958. Under local anesthesia, the left ulnar artery was exposed in the left forearm. A No. 8 cardiac catheter was introduced proximally through the artery into the aorta and advanced easily until the tip lay above the diaphragm. Blood flowed from the end of the catheter under pressure but the pulsation was dampened. The catheter was connected to an automatic pressure injector and 30 ml. of 50 per cent Hypaque was injected while a series of x-ray films were exposed. With the injection of the contrast medium the patient cried out loudly, complaining bitterly of severe tearing pain in the back. Following removal of the catheter the pain subsided and became less severe. His general condition was found to be satisfactory and the blood pressure was normal. There was mild elevation of the pulse rate. The femoral pulses were quite normal. Examination of the roentgenograms revealed the presence of dissection of the descending thoracic aorta resulting from the injection of the contrast material between the layers of the wall of the aorta above the diaphragm (Fig. 1). The appearance was that of complete aortic obstruction. A subsequent film taken 30 minutes later showed that all of the dye in the aorta had disappeared and that there was an excellent concentration of dye in the urinary bladder, attesting to the preservation of renal blood flow (Fig. 2). An x-ray film of the chest showed no change in the cardiac and aortic silhouette from that observed on admission (Fig. 3).

Pain in the back, however, continued and it was decided that operative repair of the dissection of the thoracic aorta should be performed. Hypothermia was induced by external cooling until a low temperature of 29° C. was attained 4 hours after the dissection. With the patient on the right side a left posterolateral thoracotomy was performed at the fourth interspace. The wall of the aorta was discolored with extravasated blood from the origin of the subclavian artery to the diaphragm and its pulsations were diminished. The upper portion of the descending aorta and the distal portion of the arch were mobilized. Clamps were placed across the aorta proximal to the origin of the left subclavian artery and in the mid thorax and the aorta was transected. The dissection was found to involve about two thirds of the diameter of the vessel, beginning at the origin of the left subclavian artery. On the lesser curvature of the aorta, opposite the origin of the left subclavian artery, were several atherosclerotic ulcerated areas in the intima. A ten centimeter length of the aorta, including these ulcerated areas, was excised and replaced with a pre-clotted knitted Dacron prosthesis. The false lumen was excluded both proximally and distally by suturing both layers of the aorta together to the prosthesis. The clamps were removed and the circulation restored. The immediate condition of the patient was satisfactory. Three days later a tracheostomy was performed to facilitate the removal of retained secretions from the

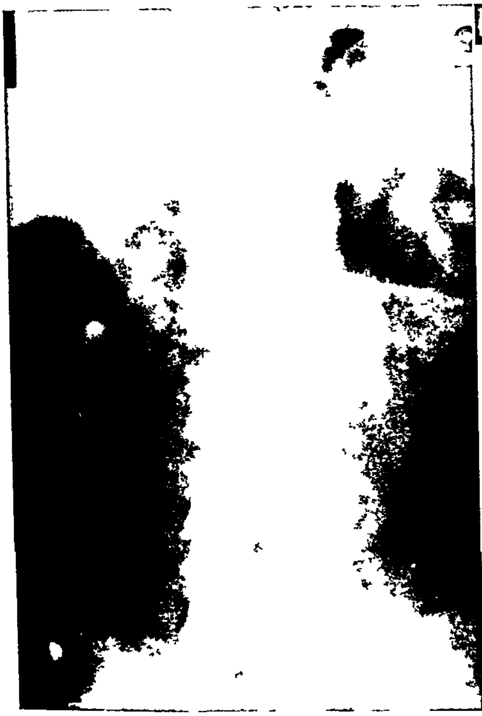

Fig 1

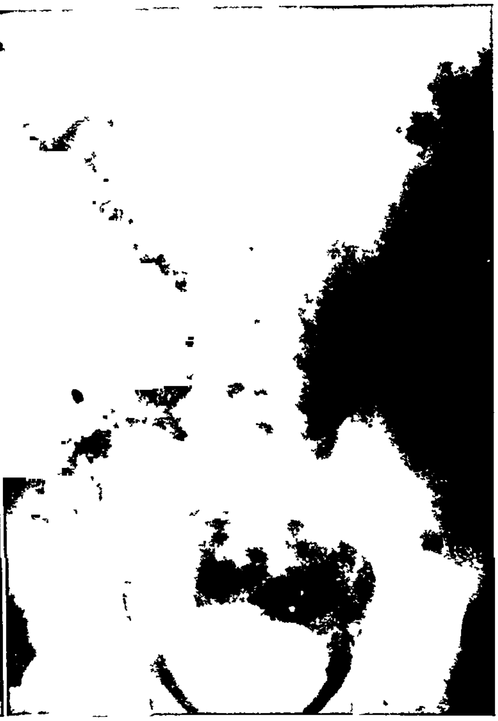

Fig 2

Fig 1 —X-ray film demonstrating radiopaque substance within the aortic wall causing transient obstruction

Fig 2 —Disappearance of radiopaque substance from the aorta and dense concentration in the urinary bladder 30 minutes after injection

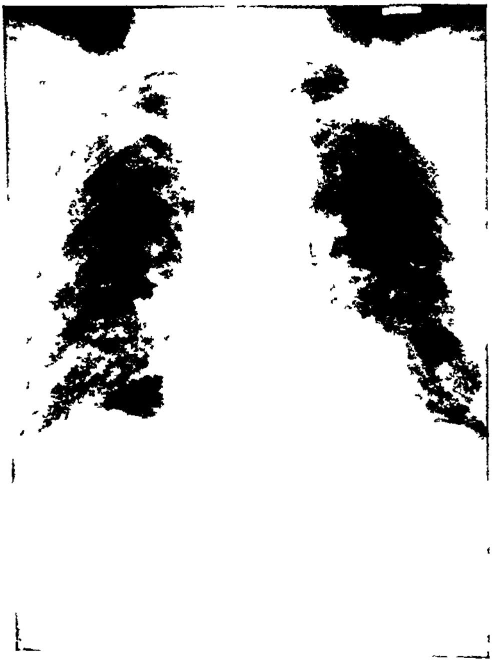

Fig 3 —Normal contour of thoracic aorta 1 hour after injection

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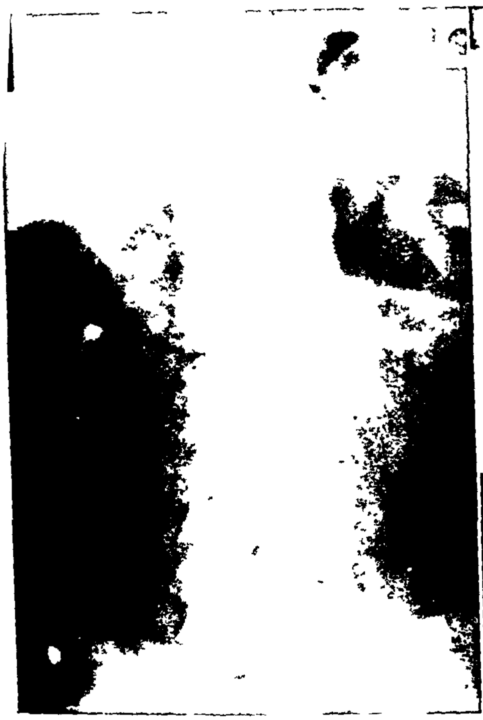
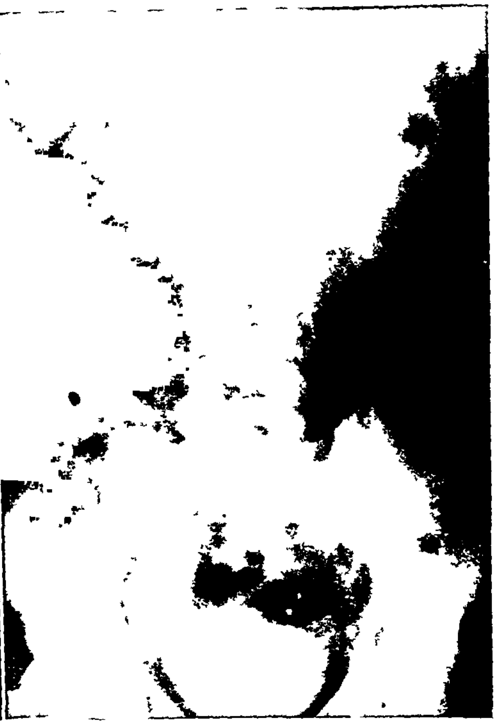


Fig. 1



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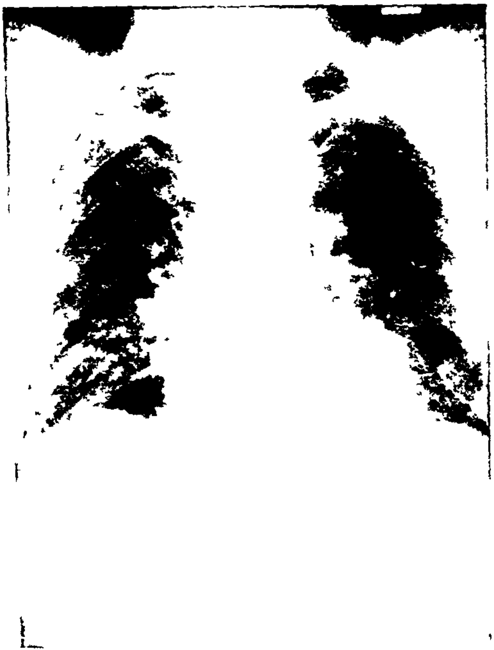

Fig 3 —Normal contour of thoracic aorta 1 hour after injection.

tracheobronchial tree. At the same time, because of poor arterial flow to the left upper extremity, the left brachial artery, which had been utilized as a pathway for the introduction of the catheter, was explored and a thrombus removed from the artery distal to the origin of the profunda branch by retrograde flush. There was no evidence of dissection in the brachial artery.

Three weeks later the patient was operated upon for his arteriosclerotic abdominal aortic aneurysm. The aneurysm was found to be large and lobulated and to arise just distal to the renal arteries. The aorta, proximal to the aneurysm, was badly diseased but there was no evidence that dissection extended below the diaphragm. The aneurysm was excised and replaced with a knitted Dacron bifurcation prosthesis.[13] The patient made a satisfactory convalescence after the resection of the abdominal aortic aneurysm and was discharged from the hospital 12 days after the last operation.

When he was seen in follow-up examination 6 months later his general condition was satisfactory. However, there was evidence of marked impairment of arterial flow to the left upper extremity. No pulses were felt distal to the left subclavian artery and there was hypesthesia and limitation of flexion of the fingers of the left hand. X-ray examination of the chest was unchanged. The lung fields were clear and only minimal widening of the aorta superiorly was noted.

DISCUSSION

The normal appearance of the aortic silhouette shortly after the production of the dissection by injection of the dye is shown in Fig. 3. The presence of the opaque material between the layers of the wall of the aorta at the completion of the injection is shown in Fig. 1. There is a sharp, right border of the opaque substance with a less definite contour to the left. There is minimal filling of the branches of the thoracic aorta, and, apparently, a complete obstruction of the aorta just above the level of the diaphragm. The dampened flow of blood from the catheter, the occurrence of severe characteristic back pain at the time of the injection of the opaque substance, and the appearance of the film leave no doubt that the dissection occurred as a result of, and at the time of, the performance of the study. The contrast material apparently was promptly removed from its position between the layers of the aortic wall as indicated by its absence from the wall on the later film and the presence of normal femoral pulses shortly after the performance of the study. Also, there was excellent excretion of the material by way of the kidneys as indicated by its presence in the urinary bladder as shown in Fig. 2.

The dissection probably occurred in the following fashion. The conventional No. 8 Lehman catheter was introduced without complication from the ulnar artery to the aorta. As it passed from the origin of the subclavian artery across the aortic lumen the tip of the catheter impinged upon one of the ulcerated areas, noted at operation, in the intima of the lesser curvature of the aorta. It was then advanced distally between the layers of the aortic wall dissecting sufficiently so that blood following it could be obtained through the catheter (Fig. 4). Only mild discomfort was experienced by the patient at this stage. The dissection was completed by the injection of the radiopaque substance under considerable pressure by means of the automatic injector (Fig. 5). It was at this time that the patient experienced the classical severe tearing pain. The extent of the dissecting aneurysm is shown in Fig. 6 and the final result in Fig. 7.

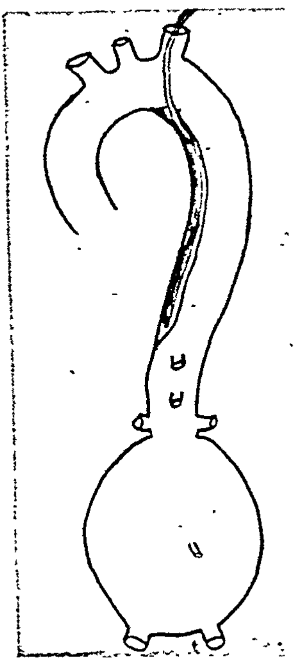

Fig. 4.

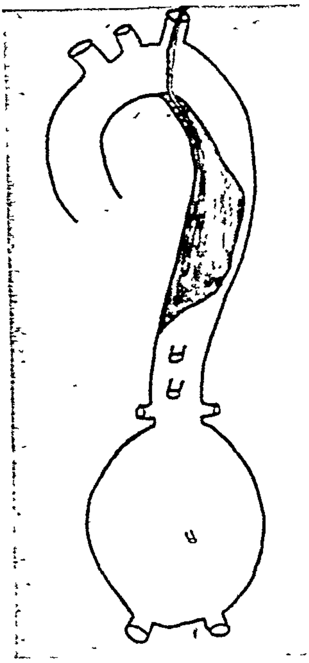

Fig. 5.

Fig. 4.—Passage of catheter through ulcerated area in the aortic wall.
Fig. 5.—Dissection produced by injection under pressure.

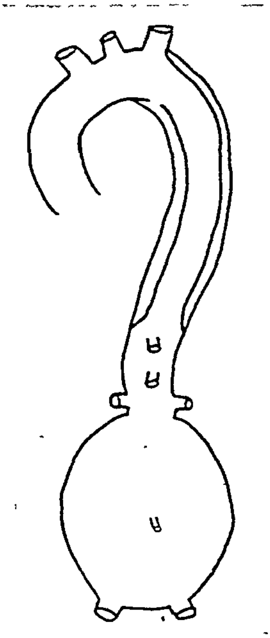

Fig. 6.

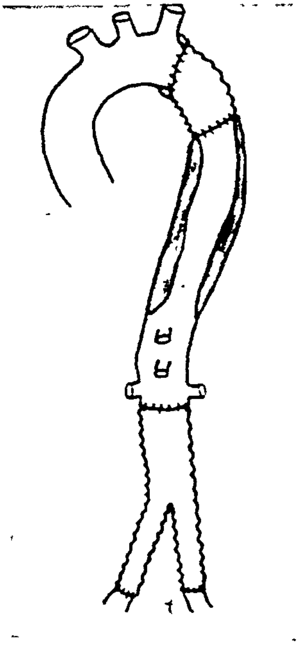

Fig. 7.

Fig. 6.—Extent of dissection.

Fig. 7.—Final result after excision and replacement of the source of the dissection, exclusion of the outer lumen proximally and distally, and resection and replacement of the abdominal aneurysm.

The poor prognosis of spontaneous dissection of the thoracic aorta and the continuation of pain in the back prompted the application of the operation for the control of dissecting aortic aneurysm described by De Bakey and his associates.[12] In this instance the location of the point of intimal perforation in an accessible area of the aorta distal to the proximal clamp permitted the performance of a curative type of operation with exclusion of the external lumen, both proximally and distally. The result achieved by this operation was such as to permit the patient to undergo successful resection of an abdominal aortic aneurysm 3 weeks later. The origin of the abdominal aneurysm distal to the renal arteries is in keeping with the characteristics of the great majority of these lesions.[2] The undesirability of performing diagnostic studies which are not necessary is obvious.

SUMMARY

The occurrence of a dissecting aneurysm of the thoracic aorta as a complication of a catheter aortogram has been described. The dissection probably occurred as the catheter tip penetrated an atherosclerotic ulcer of the intima The aneurysm was successfully treated by excision and replacement with a knitted Dacron prosthesis. Subsequently an arteriosclerotic aneurysm of the abdominal aorta was replaced with a Dacron bifurcation prosthesis. Six months later the condition of the patient was satisfactory except for impairment of arterial flow to the left upper extremity.

REFERENCES

1. Dos Santos, R., Lamas, A. C., and Caldas, J. P.: Artériographié des membres et de l'aorte abdominale, Paris, 1931, Masson et Cie.
2. Crawford, E. S., Beall, A. C., Moyer, J. H., and De Bakey, M. E.: Complications of Aortography, Surg. Gynec. & Obst. 104: 129-141, 1957.
3. McAfee, J. G., and Willson, J. K. V.: Review of Complications of Translumbar Aortography, Am. J. Roentgenol. 75: 956-970, 1956.
4. Farinas, P. L.: Una nueva technica para el examen arteriografico de la aorta abdominal y sus ramas inyectando una substancia de contraste a través de un cateter introducido por la femoral hasta aorta previa disseccion, Rev. méd. Hosp. de Mexico, October, 1940.
5. Radner, S.: Thoracic Aortography by Catheterization From Radial Artery, Acta radiol. 29: 178-180, 1948.
6. Broden, B., Jonsson, J., and Karnell, J.: Thoracic Aortography: Observation of Technical Problems Connected With Method and Various Risks Involved in Use, Acta radiol. 32: 498-508, 1949.
7. Jonsson, G., Broden, B., and Karnell, J.: Thoracic Aortography With Special Reference to Its Value in Patent Ductus Arteriosus and Coarctation of the Aorta, Acta radiol. Suppl. 89, 1-176, 1951.
8. Lane, J. D., and Peirce, E. C.: Endoaneurysmorrhaphy for Spontaneous Innominate Artery Aneurysm, Surgery 30: 709-717, 1951.
9. Deterling, R. A., Jr.: Direct and Retrograde Aortography, Surgery, 31: 88-114, 1952
10. Gaylis, H., and Laws, J. W.: Dissection of Aorta as Complications of Translumbar Aortography, Brit, M. J. 2: 1141-1146, 1956.
11. Fineberg, C., Schechter, D. C., and Barrick, C. W.: Gangrene of the Large Intestine and Ovaries After Translumbar Aortography, J. A. M. A. 167: 1232-1235, 1958.
12. De Bakey, M. E., Cooley, D. A., and Creech, O., Jr.: Surgical Considerations of Dissecting Aneurysm, Ann. Surg. 142: 586-612, 1955.
13. Crawford, E. S., De Bakey, M. E., and Cooley, D. A.: Clinical Use of Synthetic Arterial Substitutes in Three Hundred Seventeen Patients, A. M. A. Arch. Surg 76: 261-270, 1958.

EXPERIMENTAL EXCISION OF PORTIONS OF THE LEFT VENTRICLE

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A LONG-TERM study of the effects of excision of portions of the left ventricle cannot be found in the literature. With the rapid advances in cardiovascular surgery, the excision of acute infarction is now an actuality, and such a study can act as a guide as to what to expect functionally and pathologically.

Excision of acute myocardial infarcts was advocated by Murray[1] on the basis of experimental evidence in dogs. The left anterior descending coronary artery was ligated proximal to the distal two or three large terminal branches over the mid-portion of the left ventricle. This produced a lowering of the blood pressure and cardiac output with rapid progressive heart failure. After excision of the involved myocardium, the heart failure regressed and many of the dogs lived for 1 to 2 years.

Bailey and Gilman[2] excised a larger portion of the infarcted left ventricle by removing the segment involved by ligation of the left anterior descending coronary artery. All of these animals developed a heart failure syndrome similar to experimentally produced mitral stenosis. Of those surviving operation, 80 per cent died of heart failure. Carter and MacMillan[3] excised apical portions of the left ventricle in 25 dogs with 13 surviving for long-term study. There was no impairment of cardiac function or emboli in these animals.

The purpose of this study was to observe the effects on the heart of excision of portions of the left ventricle. As Bailey and Gilman's work showed a limitation in the amount of the left ventricle which could be excised, small areas were intentionally removed in order to obtain long-term survival for follow-up study.

METHODS

Mongrel dogs were used, varying in weight from 7.6 to 26.8 kilograms. Nembutal anesthesia was induced and the trachea intubated. A cuff on the endotracheal tube was inflated and carefully checked for leakage. The expired air was collected in Douglas bags after passage through a gas meter. Arterial

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blood samples were collected from a femoral artery catheter. A cardiac catheter was placed into the right ventricle through a femoral vein cut down, and was positioned by observing the right ventricular pressure curve on a Sanborn recorder. Expired air oxygen concentration was determined with a Beckman O_2 analyzer. Arterial and venous oxygen concentrations were determined by the method of Hickam and Frayser.[4] The cardiac output was then determined by the Fick principle.

After obtaining an initial cardiac output, the left side of the chest was opened and one of the large branches of the left anterior descending or left circumflex coronary artery was tied off. The area of cyanosis and paradoxical motion was observed and this outlined the area for excision. This usually amounted to an oblong area about 4 cm. long and 2 cm. wide. The surrounding normal-appearing muscle was approximated with mattress sutures of No. 1-0 chromic catgut on a large, curved, swaged-on needle. A continuous No. 1-0 silk arterial suture was then placed at the distal end of the puckered myocardium; as the myocardium was excised with small scissors, the continuous over-and-over suture was advanced. The pericardium was loosely closed, and the thoracotomy wound was closed in layers over a large catheter. The pleural cavity was aspirated well and the chest catheter was removed. Samples were then obtained for a repeat cardiac output. Subsequent determinations of cardiac output were done in a manner similar to the initial output.

An adequate depth of anesthesia was found to be necessary to prevent forceful expiration by the dog against the inflation phase of the respirator with loss of air from the system. Right ventricular samples were used instead of the pulmonary artery, since samples could seldom be withdrawn successfully from the pulmonary artery.

CLINICAL COURSE

Twenty-two dogs had an area of the heart excised which was made cyanotic by ligation of a branch of the left anterior descending coronary artery, and 10 dogs had an area of the heart excised after ligation of a branch of the left circumflex coronary artery. The causes of death are shown in Table I.

TABLE I. CAUSE OF DEATH OF 32 DOGS OPERATED UPON

	BRANCH OF LEFT ANTERIOR DESCENDING CORONARY LIGATED	BRANCH OF LEFT CIRCUMFLEX CORONARY LIGATED
Number of animals	22	10
Rupture of heart	6	1
Empyema	2	2
Atelectasis	3	0
Fibrillation at operation	3	0
Congestive failure	0	1
Aspiration pneumonia	1	1
Undetermined	1	1
Sacrificed	6	4

Nine dogs were operated upon as controls; 4 had a branch of the left anterior descending coronary artery ligated, and were observed to have an area of cyanosis and paradoxical motion; 5 dogs had a sham operation consisting of a left thoracotomy, opening of the pericardium, and manipulation of the heart, so that the time of operation was equivalent to the time necessary for excision of a portion of the myocardium.

Of the group which had a branch of the left anterior descending coronary artery ligated, 6 died of rupture of the heart between 4 and 12 days postoperatively. One of these dogs developed areas of skin necrosis from arterial emboli. Two dogs died of empyema on the fifth and fourteenth days; 3 of atelectasis on the first, second, and fourth postoperative day. Three dogs died at the time of operation from ventricular fibrillation. One dog died 2 months after operation from aspiration pneumonia following anesthesia for coronary arteriograms. One dog died 4 days after operation from an undetermined cause. Six dogs were sacrificed at 5, 6, 7, 12, 15, and 27 months after operation.

Of the group which had a branch of the left circumflex coronary artery ligated, 1 died of rupture of the heart 7 days postoperatively, and 2 died of empyema on the fifth and fourteenth days. One dog died of congestive heart failure 13 weeks after operation. This dog (C 27) had had a repeat cardiac output 1 day prior to death, at which time 4 L. of abdominal ascitic fluid were withdrawn. Autopsy showed mitral insufficiency due to the posterior papillary muscle being caught in the suture line. One dog (C 26) died 10 weeks after ventricular resection of aspiration pneumonia the day after a repeat cardiac output. One dog died on the first postoperative day of an undetermined cause. The remaining 4 dogs were sacrificed at 1, 2, 5, and 7 months.

The 4 control dogs, which had the branch of the left anterior descending coronary artery ligated, all did well after operation. One was autopsied at 3 weeks; 2 were autopsied at 4 weeks; and 1 was autopsied at 6 weeks.

The 5 control dogs which had sham operations did well after operation; 3 were not followed, and 2 were autopsied at 3 weeks.

TABLE II. CARDIAC OUTPUT IN LITERS PER MINUTE IN DOGS WHICH SURVIVED FOR REPEAT DETERMINATION*

DOG NUMBER	WEIGHT (KG.)	INITIAL	POSTOP.	2-3 WEEKS	4-6 WEEKS	8-13 WEEKS	20-28 WEEKS
C 10	10.0	2.7	1.5		2.6		
C 15	20.0	5.9	4.7		4.0		4.3
C 16	13.6	3.2	1.8	1.6			
C 20	21.1	5.4	1.8	3.0			4.5
C 23	26.8	7.1	2.4		2.7		4.2
C 25	19.1	4.5	2.7	1.5	3.5		2.9
C 26	7.6	0.6	0.4	2.0		3.1	
C 27	10.5	2.7	0.9		2.0	1.0	
C 28	20.9	5.6	1.4	1.6			
C 30	10.0	3.5	.7	3.0	1.8	5.6	
C 31	19.2	3.8	2.9	3.1		3.4	

*The first 5 dogs listed above had an area excised supplied by branches of the left anterior coronary artery and the subsequent 6 had an area excised supplied by branches of the left circumflex coronary artery. C 26 which was a young dog, grew during its period of observation from 7.6 Kg. to 14.5 Kg C 27 also gained weight during its period of observation. This weight gain is accounted for by the fluid retention from congestive heart failure.

CARDIAC OUTPUTS

The data for the cardiac output findings in those animals which had them repeated at intervals after operation are shown in Table II.

The data for those dogs which had only a preoperative and immediate postoperative cardiac output done are shown in Table III. All but 4 of the 27 dogs with pre- and postoperative cardiac outputs showed a drop in cardiac output immediately after operation. A tendency was apparent for the cardiac output to increase with time after resection. In 1 case (C 27) congestive failure developed, and a subsequent fall in cardiac output was noted 13 weeks postoperatively. One dog (C 26) was a 7.6 kilogram puppy at the time of operation, and at the time of the last cardiac output weighed 14.5 kilogram. In this dog both subsequent cardiac outputs exceeded the initial level.

TABLE III. CARDIAC OUTPUT IN LITERS PER MINUTE IN DOGS WHICH DID NOT SURVIVE FOR REPEAT DETERMINATION

DOG NUMBER	WEIGHT (KG.)	CO L./MIN. (INITIAL)	CO L./MIN. (POSTOP.)	PORTION OF VENTRICLE EXCISED
C 5	12.0	2.4	2.3	LAD[*]
C 6	15.0	1.0	0.5	LAD
C 7	23.2	4.8	1.3	LAD
C 8	15.4	3.9	1.2	LAD
C 9	9.3	0.7	0.7	LC[†]
C 11	12.3	1.3	1.9	LAD
C 12	15.0	2.0	1.0	LAD
C 13	17.0	1.5	1.1	LAD
C 14	15.0	3.2	1.8	LAD
C 17	13.1	3.0	1.3	LAD
C 18	18.9	2.9	1.1	LAD
C 19	12.5	1.6	1.2	LAD
C 21	18.2	3.4	0.7	LAD
C 22	19.5	2.3	1.9	LAD
C 29	22.7	6.1	6.4	LC
C 32	10	0.9	0.4	LC

[*] LAD = Area of heart supplied by branches of the left anterior descending coronary artery.

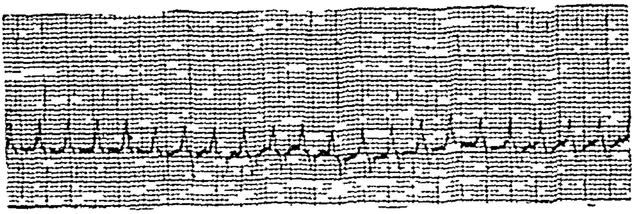
[†] LC = Area of heart supplied by branches of the left circumflex artery.

The data for the control group is shown in Table IV. In all 4 of the dogs which had the branch of the coronary artery ligated, there was a significant drop in the cardiac output. The 1 dog which had a return to normal cardiac output in 2 weeks had no evidence of infarction at autopsy 3 weeks after operation (CA 79). Dog B 12 had a return to preoperative cardiac output at 4 weeks, and at autopsy was found to have an infarction which was small and extended only about halfway through the thickness of the myocardium. Dogs CA 52 and CA 74 did not have a return of the cardiac output to preoperative levels at 4 weeks and 6 weeks postoperatively. At autopsy both were found to have healing infarcts involving the full thickness of the myocardium.

Of the group of 5 dogs which had sham operations, only 1 (B 7) had a significant fall in cardiac output immediately after operation. There was a return to preoperative output at 2 weeks.

TABLE IV. CARDIAC OUTPUTS IN LITERS PER MINUTE ON CONTROL DOGS

DOG NUMBER	WEIGHT (KG.)	INITIAL	IMMEDIATELY POSTOP.	2 WEEKS POSTOP.	4 WEEKS POSTOP.	6 WEEKS POSTOP.
Coronary Artery Branch Tied						
CA 79	11.3	2.2	1.3	3.2		
CA 74	7.7	1.7	0.9	1.3	1.0	
B 12	9.1	2.1	1.2	1.3	2.1	
CA 52	18.6	6.0	3.6	3.2	4.0	4.2
Sham Operation						
B 7	12.7	4.0	2.4	4.4		
CA 85	23.2	3.4	3.1	5.7		
B 5	10.9	3.1	2.9			
81	10.4	2.3	2.3			
36	11.8	1.4	1.2			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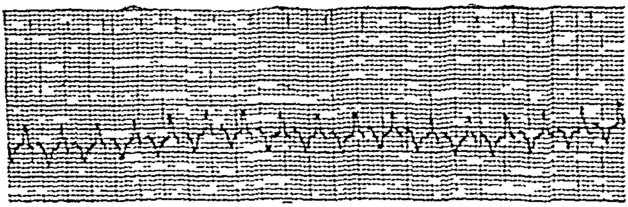
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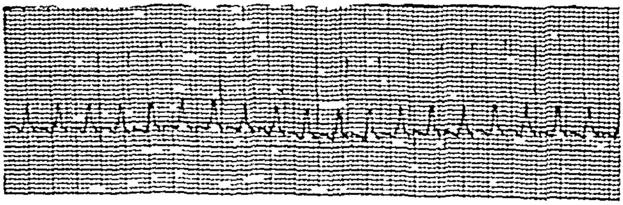

6 WEEKS AFTER EXCISION 18 JUNE 1958

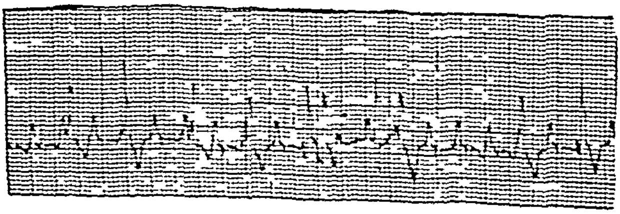
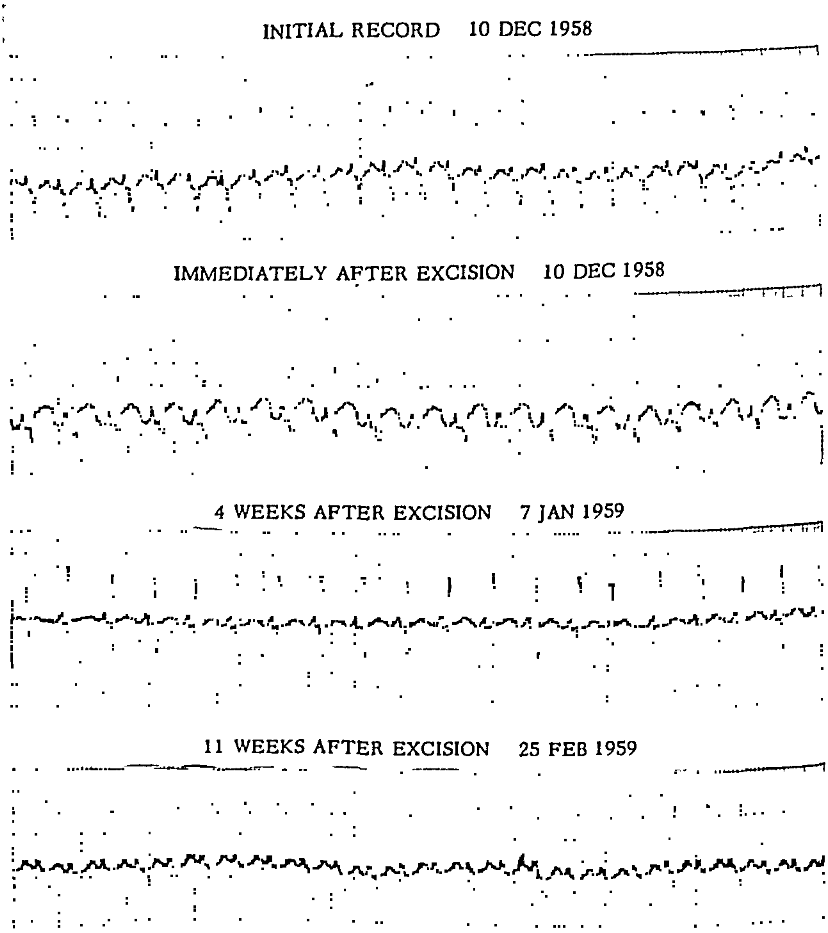

DURING POSITIONING OF CATHETER 18 JUNE 1958

FIG 1.—Lead III of the electrocardiogram in Dog C 10 demonstrates the minimal changes associated with ligation of the branches of the left anterior descending coronary artery and excision of the cyanotic portion of the myocardium.

ELECTROCARDIOGRAPHIC CHANGES

The electrocardiographic changes were not striking in the group which had branches of the left anterior descending coronary artery ligated, and range from no significant change to T-wave inversion and slight S-T segment widening. Fig. 1 shows the changes in Lead III which occurred in Dog C 10. A period of a large number of ventricular complexes which occurred during positioning of the cardiac catheter in the right ventricle is also shown. This was found to occur in practically every one of 32 animals studied, but to a much less degree.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4 WEEKS AFTER EXCISION 7 JAN 1959
11 WEEKS AFTER EXCISION 25 FEB 1959

Fig. 2.—Lead III of the electrocardiogram in Dog C 30 demonstrates the acute injury pattern after ligation of a branch of the left circumflex coronary artery and excision of the cyanotic area of myocardium. Note the recovery at 4 weeks.

In the group which had ventricular resection after a branch of the left circumflex artery was ligated, more striking changes were found. These changes were an acute injury pattern with S-T elevation and T-wave inversion as shown in Fig. 2.

In the control group with ligation of a branch of the anterior descending coronary artery, there were minor electrocardiographic changes similar to those seen in the excision group. These changes had all reverted to normal by the second week after ligation.

In the control group with a sham operation, only 1 of the 5 showed electrocardiographic changes. This dog (CA 85) had 30-second occlusion of a large proximal branch of the left anterior descending coronary artery, and developed an acute injury pattern which had reverted to normal within 30 minutes.

In both the operative and control group, the electrocardiographic changes had returned to normal within 2 weeks.

VENTRICULAR FIBRILLATION

Ventricular fibrillation occurred six times. On the first two occasions, an electrical defibrillator was not available and both dogs died. Electrical defibrillation was successful in the other 4, but 1 dog did not recover satisfactory heart efficiency and died within an hour. Fibrillation occurred once prior to ligation and the others within 30 minutes after coronary artery ligation. Ventricular fibrillation did not occur in the control group.

BLOOD PRESSURE

There was no precipitous drop in blood pressure that correlated with ligation of the coronary artery. Twenty-seven dogs had the blood pressure recorded before, during, and after the operative procedure. In 18 of these, there was a transient fall in blood pressure associated with manipulation of the heart. This averaged about 65 mm. Hg fall in the systolic blood pressure. In 9, there was a transient average rise of blood pressure of 9 mm. Hg. By the end of the procedure there was an average fall in the systolic blood pressure of 55 mm. Hg in 24 of the dogs. Three had an average rise of 10 mm. Hg in the systolic blood pressure at the end of the procedure, and 2 of these 3 also did not have a fall in the cardiac output. Conversely, of the 4 dogs which did not have a drop in the cardiac output at the end of the procedure, 2 had a rise in the systolic blood pressure, and the other 2 did not have the blood pressure measured. In those dogs which had subsequent cardiac outputs done, the lowered systolic blood pressure had returned to normal preoperative levels in all but 3 (C 23, C 27, and C 28).

In the control group with ligation of a branch of the left anterior descending coronary artery, there was no fall in the blood pressure associated with the actual vessel ligation. There was an average fall in the systolic blood pressure in these 4 dogs of 40 mm. Hg from beginning to end of the operation. Two weeks after operation there was an average rise in the systolic blood pressure of 15 mm. Hg above the preoperative level.

In the control group with a sham operation, there was an average fall in systolic pressure of 20 mm. Hg below the preoperative levels.

DISCUSSION

The high incidence of disruption of the cardiac wounds found at autopsy was due to strangulation of the tissues by the mattress suture technique. This finding was also demonstrated by Carter and MacMillan.[3] The lower rate of wound disruption in those dogs which had areas excised that were supplied by branches of the left circumflex coronary artery was probably due to the partial covering effect of the posterior papillary muscle over the myocardial wound. A two- and three-layer closure of continuous sutures with the aid of extracorporeal circulation gives a much more satisfactory approximation of the wound edges. None of the 3 dogs, however, closed in this manner survived beyond the first postoperative day due to brain damage, and no long-time wound studies have been done. Our experience with one human case, using a mattress type of suture technique for a large ventricular aneurysm, resulted in a false aneurysm developing at the suture line which required re-operation in 4 months.

Congestive heart failure was not a problem in these dogs which was probably because of the small area of myocardium involved. There was 1 dog in which decompensation did develop and this was thought to be due to mitral insufficiency from catching and fixing the chordae tendineae of the mitral valve in the suture line.

The cardiac output was shown to fall in the control group from ligation of a coronary artery, if an area of cyanosis and absence of contraction was produced. It was also shown in this group that if infarction was not produced (CA 79) or if the area of infarction was small and did not involve the full thickness of the myocardium (B 12), the return to preoperative output was rather rapid, within 2 to 4 weeks. Normal function did not return within 4 to 6 weeks in 2 dogs which had an infarction involving the full thickness of the myocardium. These findings in the control group substantiate the findings in the operative group (see Table II) which was followed for many months. At autopsy the myocardial scar was similar in size and appearance to the scar produced by infarction from ligating a coronary artery. The control group of sham operations demonstrated that thoracotomy and manipulation of the heart affect the cardiac output very little.

The electrocardiographic changes which in some cases were very striking did not persist for long. All animals were restudied within 2 to 6 weeks after operation. In every dog which survived for follow-up study, the electrocardiogram had returned to normal.

No correlation could be found between the blood pressure changes and cardiac output which was not surprising, in view of the mechanisms of blood pressure control.

SUMMARY AND CONCLUSIONS

Thirty-two dogs had a branch of the coronary artery ligated which produced a small area of cyanosis over an area of the left ventricle. The area of cyanosis was excised, and the animals studied at intervals before and after operation for changes in the clinical course, cardiac output, blood pressure, electrocardiogram, and morphologic changes in the heart. One control group of 4 dogs with various branches of the coronary arteries ligated was studied in a similar manner as was another control group of 5 dogs with a sham operation.

Ligation alone or ligation with excision of the cyanotic myocardium produced similar changes in the cardiac output, electrocardiogram, and morphology of the myocardium. Thoracotomy and manipulation of the heart produced little or no changes in the areas investigated in a control group of animals.

There appears to be no advantage to excising an area of small acute myocardial infarction in which the resulting scar will be as large as the scar from the healing infarct. The mattress suture technique used in these experiments is unsatisfactory due to strangulation of the myocardium and frequent rupture of the suture line.

REFERENCES

1. Murray, G.: The Pathophysiology of the Cause of Death From Coronary Thrombosis, Ann. Surg. 126: 523-534, 1947.
2. Bailey, C. P., and Gilman, R. A.: Experimental and Clinical Resection for Ventricular Aneurysm, Surg. Gynec. & Obst. 104: 539-542, 1957.
3. Carter, B. N., and MacMillan, B. G.: Technique for Excision of Portions of the Entire Thickness of the Ventricles of the Heart, An Experimental Study, Surg. Gynec. & Obst. 90: 282-290, 1950.
4. Hickam, J. B., and Frayser, R.: Spectrophotometric Determination of Blood Oxygen, J. Biol. Chem. 180: 457-465, 1949.
5. Greenfield, J. C., Jr., and Dillon, M. L., Jr.: Hemorrhagic Pericardial Effusion Following Myocardial Infarction Associated With a Ventricular Aneurysm, Am. Heart J. 57: 327-332, 1959.

EXPERIMENTAL TEFLON REPLACEMENT OF THE SUPERIOR VENA CAVA AND ATRIOCAVAL JUNCTION

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INTRODUCTION

Continuing study of suitable replacements for the superior vena cava and its atrial junction is advisable because of the serious consequences of occlusion[19] of these structures by neoplasm,[1] inflammatory conditions, or trauma If the block is short, excision and direct anastomosis of the superior vena cava to the right atrium has been shown to be feasible by Gerbode and colleagues,[7, 8] and more recently by Riberi and Moore.[23] For the management of longer blocks, Sauvage and Wesolowski,[24] Scannell and Shaw,[25] and Schauble and associates[9] have reported satisfactory results with the use of venous grafts, while other authors[3] did not find vein grafts satisfactory. In 1954, Holman and Steinberg[18] reported successful relief of human superior vena caval occlusion using an homologous arterial graft, while Ohara and Sakai,[22] and MacLean and associates[21] concluded that such arterial segments were unsatisfactory in dogs. Many different fabrics of plastic material have been employed to replace veins. Nylon, Dacron, Orlon, and Ivalon fabrics or polyethylene tubes are not satisfactory materials for use as experimental venous prostheses according to reports by Egdahl, Hume, and Schlang,[5, 6] Deterling and Bhonslay,[3, 4] and MacLean and colleagues.[21]

From these reports it would appear that the successful grafting of great veins is considerably more capricious than is the replacement of arterial segments. The relatively slow venous blood flow and the ease of mechanical distortion of suture lines in the low pressure venous system must contribute to the poor results obtained when grafts or prosthetic materials are placed to bridge venous defects.

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Recent reports on the surgical characteristics of the new tetrafluorethylene fabric, Teflon, have suggested that this material might prove superior to other prostheses applied to the venous system. Teflon has performed well when used for arterial replacement[9-11, 13-17] and it has been apparent from the studies of Girvin and his co-workers,[9] Harrison,[13, 14] and LeVeen and Barberio[20] that the substance causes minimal tissue reaction. Consequently, we have undertaken an experimental study of superior vena caval replacement with this type of fabric tube.

METHODS

Stock mongrel dogs, varying in weight from 10 to 15 Kg., were anesthetized with Pentothal administered intravenously in concentrations of 25 mg. per kilogram of body weight. A right thoracotomy was carried out. The superior vena cava and upper portion of the right atrium were exposed by incision of the mediastinal pleura and pericardium. Care was taken to avoid injury to the adventitial planes of the vena cava. The azygos vein was divided between ligatures. Potts ductus clamps were applied to the vena cava or atrium, suitable segments of the vessel excised, and prosthetic replacement carried out. The prosthetic device inserted was the crimped, woven, tetrafluorethylene fabric, 12 mm. in diameter.[*] The grafts were not preclotted. The field was moistened with saline solution but anticoagulants were not used.

In one group of animals, segments of the superior vena cava, varying in length from 2 to 4 cm., were excised and were replaced by the fabric. The anastomoses were carried out by continuous glover's suture of atraumatic 4-0 silk.

In the second group of animals, similar lengths of the superior vena cava were excised including the atriocaval junction; the atrial defect was closed with sutures, and the Teflon prosthesis connected between the distal superior vena cava and a linear defect placed in the side of the right atrium immediately adjacent to the atriocaval junction.

Postoperatively the animals were given injections of penicillin and streptomycin for a period of several days and were then placed on full activity in an animal run.

RESULTS

We have placed 30 grafts in defects in the superior vena cava. Of these animals, 11 died between 1 and 60 days after operation, 5 died of postoperative shock within 24 hours, 3 died of empyema, and 3 died of hydrothorax secondary to thrombosis of the graft and progressive deterioration. The development of graft thrombosis was demonstrated by a loss of vitality, appetite, and hair, and ventilatory disturbance. In the 8 animals that died of shock and empyema, one graft was partially obstructed by thrombus and seven were found to be completely patent.

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[*] Edwards-type Teflon arterial graft, manufactured by the United States Catheter and Instrument Co, Glens Falls, New York; distributed by C R. Bard, Inc, Summit, N. J.

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INTRODUCTION

Continuing study of suitable replacements for the superior vena cava and its atrial junction is advisable because of the serious consequences of occlusion[19] of these structures by neoplasm,[1] inflammatory conditions, or trauma If the block is short, excision and direct anastomosis of the superior vena cava to the right atrium has been shown to be feasible by Gerbode and colleagues,[7, 8] and more recently by Riberi and Moore.[23] For the management of longer blocks, Sauvage and Wesolowski,[24] Scannell and Shaw,[25] and Schauble and associates' have reported satisfactory results with the use of venous grafts, while other authors[3] did not find vein grafts satisfactory. In 1954, Holman and Steinberg[15] reported successful relief of human superior vena caval occlusion using an homologous arterial graft, while Ohara and Sakai,[22] and MacLean and associates[21] concluded that such arterial segments were unsatisfactory in dogs. Many different fabrics of plastic material have been employed to replace veins. Nylon, Dacron, Orlon, and Ivalon fabrics or polyethylene tubes are not satisfactory materials for use as experimental venous prostheses according to reports by Egdahl, Hume, and Schlang,[5, 6] Deterling and Bhonslay,[3, 4] and MacLean and colleagues.[21]

From these reports it would appear that the successful grafting of great veins is considerably more capricious than is the replacement of arterial segments. The relatively slow venous blood flow and the ease of mechanical distortion of suture lines in the low pressure venous system must contribute to the poor results obtained when grafts or prosthetic materials are placed to bridge venous defects.

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***Department of Surgery, Lahey Clinic, Boston, Mass, and Consultant in Surgery and Physiology, U S Naval Hospital, Chelsea, Mass marked narrowing as a result of the contracture of the anastomosis. The three completely obstructed grafts have revealed thrombosis involving the entire prosthesis (Table I).

A graft was placed at the atriocaval junction in 7 animals. Four animals died between 1 and 22 days after operation, 2 died of postoperative shock, and 2 of hydrothorax resulting from total prosthesis thrombosis. Of the 3 survivors, one graft was patent after 1 month, and two grafts were narrowed by contracture of the atrial suture line at 3 and 6 months, respectively, after operation. In 2 of the nonsurvivors, the grafts were completely obstructed at 7 and 22 days after operation (Table II).

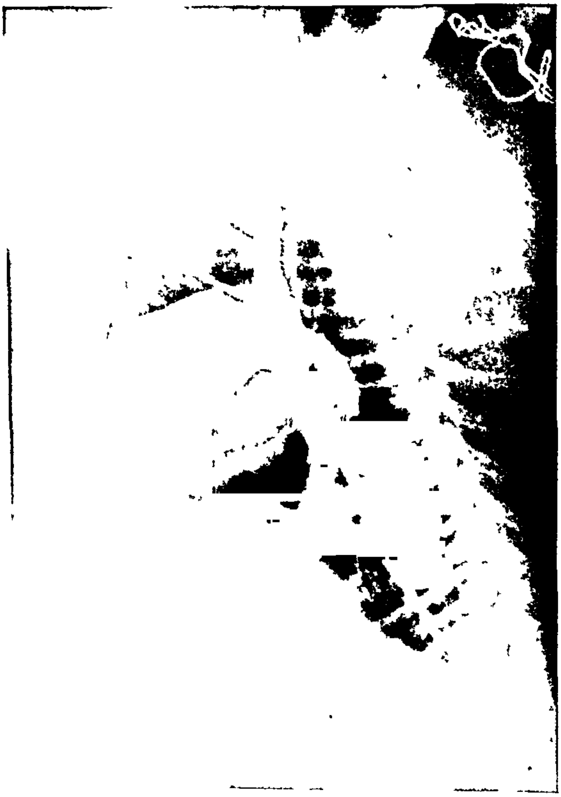

Fig 3.—Venogram illustrating wide patency of a cavo-caval Teflon prosthesis at 10 months.

TABLE II. ATRIOCAVAL JUNCTION GRAFTS (TOTAL FOLLOW-UP)

TIME AFTER OPERATION	NUMBER	PATENCY	PARTIAL OBSTRUCTION	TOTAL OBSTRUCTION
24 hr.	2	2	0	0
1 wk.	1	0	0	1
3 wk.	1	0	0	1
1 mo.	1	1	0	0
3 mo.	1	0	1	0
6 mo.	1	0	1	0
Totals	7	3	2	2

Of 19 long-term survivors in apparent normal health, ten grafts have been completely patent, six partially narrowed, and three thrombosed completely. Of the ten patent grafts, three showed slight narrowing of the anastomosis without consequence to the blood flow through the graft. Of the six grafts that became partially occluded, four have shown a small thrombosis and two a

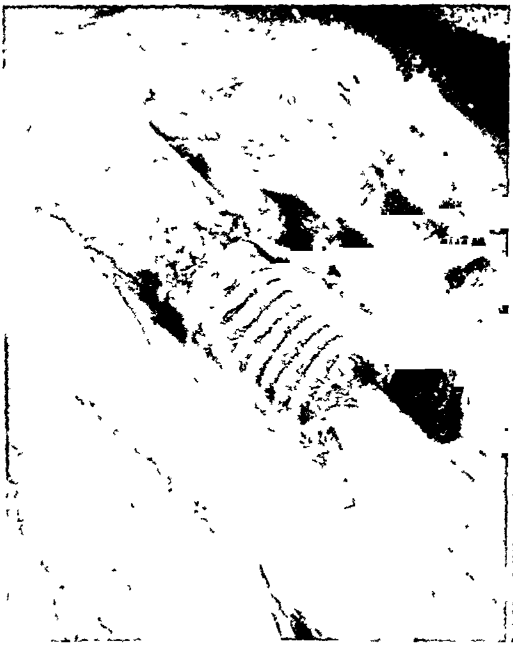

Fig. 1

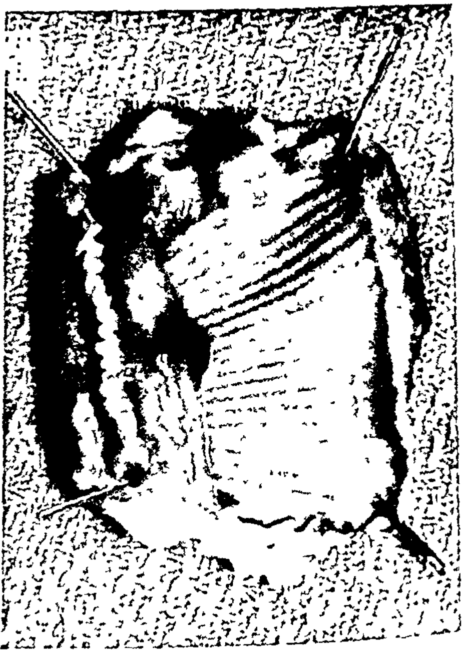

Fig 2.

Fig. 1.—Teflon prosthesis in situ in the superior vena cava 9 months after operation Absence of significant tissue reaction about the graft is apparent. Prosthesis is stiff enough to hold the lumen of the vena cava open along each suture line

Fig 2.—Interior of the same prosthesis. Suture line is not contracted at either end of the prosthesis

TABLE I. SUPERIOR VENA CAVAL GRAFTS (TOTAL FOLLOW-UP)

TIME AFTER OPERATION	NUMBER	PATENCY	PARTIAL OBSTRUCTION, NARROWING, OR THROMBOSIS	TOTAL OBSTRUCTION BY THROMBOSIS
24 hr.	5	5	0	0
5 da.	1	1	0	0
1 wk.	2	1	1	0
2 wk.	3	2	0	1
3 wk.	1	1	0	0
1 mo.	1	0	1	0
2 mo.	3	1	0	2
3 mo.	1	0	1	0
4 mo.	1	0	1	0
5 mo.	2	1	0	1
6 mo.	2	1	1	0
7 mo.	2	1	0	1
8 mo.	2	1	1	0
9 mo.	2	1	0	1
10 mo.	2	1	1	0
Totals	30	17	7	6

DISCUSSION

Teflon fabric was easy to suture and the edge of the vessel and graft was well everted by a single, continuous glover's suture line. The corrugated nature of the tube would appear to present advantages in maintaining patency after venous anastomosis since such a fabrication has a stentlike action on luminal shape and suture lines are well separated. The importance of holding an atriocaval anastomosis open has been emphasized by Benvenuto and Lewis.[2] A similar stenting action may account for the success of an Ivalon-Lucite prosthesis placed by MacLean and colleagues[21] in the inferior vena cava.

It has been shown by Harrison and co-workers[12, 17] and LeVeen and Barberio[20] that Teflon causes minimal tissue reaction and this has been confirmed by our own study. There is little fibrotic reaction along the exterior walls of the prosthesis and complete absence of collapse of the prosthesis secondary to external compression.

Ivalon, Dacron, nylon, and Orlon used as venous prostheses have been widely studied by Deterling and Bhonslay,[5] Egdahl,[6] and MacLean and associates,[21] Ohara and Sakai,[22] Sauvage and Wesolowski,[24] and Schauble and co-workers[25] and have been found generally unsatisfactory because of a tendency to become obstructed by early thrombosis. In comparison with these studies, we have found Teflon to have a higher patency rate. There has been no time limit at which all grafts have become occluded. Obstruction by thrombosis has occurred between 1 week and 10 months.

When a graft has thrombosed gradually, development of collateral circulation has usually been sufficient to allow adequate superior caval return to the heart. When total graft obstruction was present, it was always secondary to thrombosis originating at a suture line. In some instances, narrowing has been found to occlude the graft partially, usually at only one end of the prosthesis. In no instance has associated collapse of the prosthesis been noted and, when thrombosed, it has remained free of contracture and has retained its original shape.

The general appearance and behavior of the animals usually indicated that a graft was becoming obstructed. Edema of the head and upper extremities has not occurred, but there has been a loss of vitality and weight. The absence of edema and slow progression of other signs have been considered secondary to the extensive collateral circulation developed.

In conjunction with the finding of a relatively low incidence of occlusions (all arising at the suture line), it must be remembered that the human being does not possess as active a coagulation mechanism as the dog so that minor irregularities in the suture lines would be more likely to cause thrombosis in the dog than in the human being. These facts have led us to believe that the larger Teflon prostheses required for human superior caval replacement would be even more likely to succeed. We have placed two such prostheses in human beings and have been favorably impressed by their initial characteristics. Details of the operative procedures and long-term follow-up will be presented in a future publication.

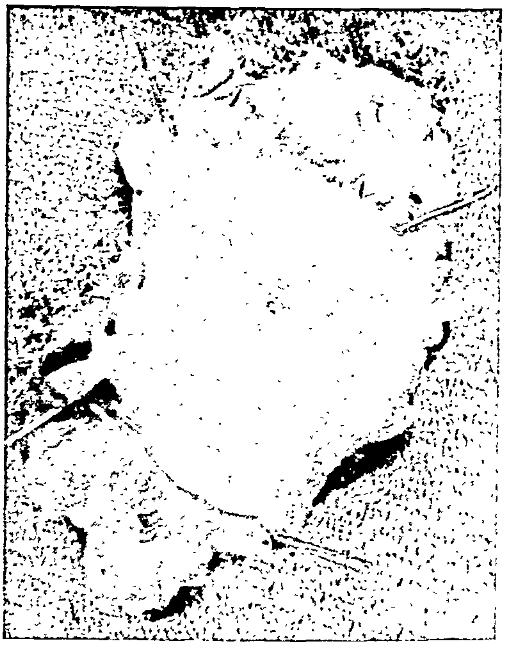

Fig. 4.—Atriocaval prosthesis at 6 months. There is evidence of moderate contracture of the atrial suture line, but the graft is completely endothelized and patent. This degree of narrowing at the atrial suture line would be classified as "partial occlusion."

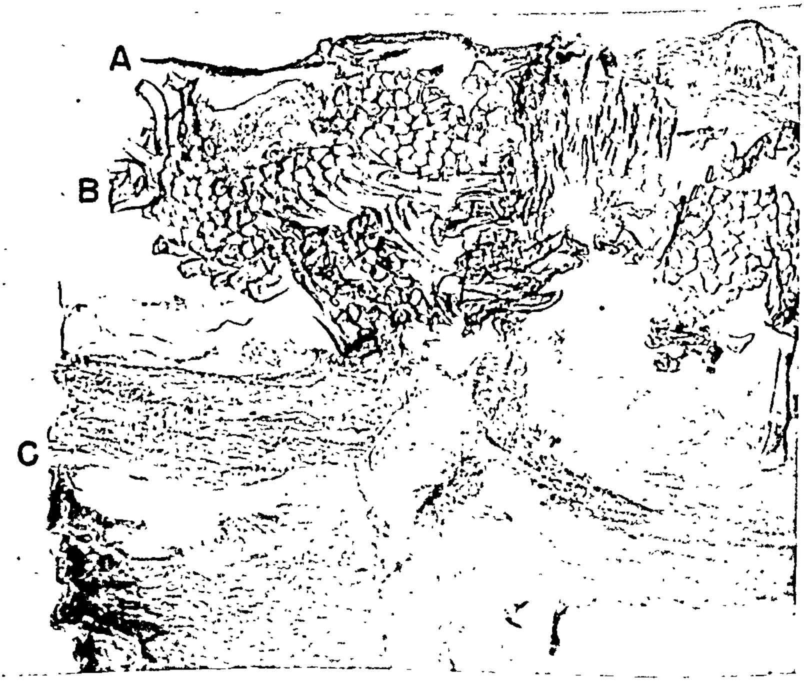

Fig. 5.—Teflon prosthesis at 9 months (×100; reduced ⅑₀). *A*, Endothelial surface; *B*, Teflon; *C*, perivascular fibrous tissue. Note the absence of tissue reaction about the plastic fabric.

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SUMMARY

The superior vena cava and atriocaval junction have been replaced in a series of dogs by Edwards-type, Teflon arterial graft fabric. After a follow-up period of 10 months of thirty grafts in the superior vena cava, seventeen have been found patent, seven partially obstructed, and six totally obstructed. During the same period, three of seven atriocaval grafts have been found to remain patent, one has been partially obstructed, and three totally obstructed.

We are indebted to Mr. Norman Jeckel of the United States Catheter and Instrument Co., Glens Falls, New York, and Mr. Alfred B. Beers of the C. R. Bard Inc., for the Teflon prostheses used in this study.

REFERENCES

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6. Egdahl, R. H., Hume, D. M., and Schlang, H. A.: Plastic Venous Prostheses, S. Forum 5: 235-241, 1955.
7. Gerbode, F., and Hultgren, H. N.: Observations on Experimental Atriovenous Anastomoses, With Particular Reference to Congenital Anomalies of Venous Return to Heart, and to Cyanosis, Surgery 28: 235-244, 1950.
8. Gerbode, F., Yee, J., and Rundle, F. F.: Experimental Anastomoses of Vessels to Heart; Possible Application to Superior Vena Caval Obstruction, Surgery 25: 556-565, 1949.
9. Girvin, G. W., Wilhelm, M. C., and Merendino, K. A.: The Use of Teflon Fabric as Arterial Grafts; An Experimental Study in Dogs, Am. J. Surg. 92: 240-247, 1956.
10. Girvin, G. W., Schlosser, R. J., Eade, G. G., and Merendino, K. A.: Teflon Fabric Grafts in Growing Pigs, Surgery 42: 710-716, 1957.
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16. Harrison, J. H.: Synthetic Materials as Vascular Prostheses. III. Long-term Studies on Grafts of Nylon, Dacron, Orlon, and Teflon Replacing Large Blood Vessels, Surg. Gynec. & Obst. 108: 433-438, 1959.
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18. Holman, C. W., and Steinberg, I.: Treatment of Superior Vena Caval Occlusion by Arterial Graft; Preliminary Report, J. A. M. A. 155: 1403-1405, 1954.
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A SIMPLIFIED TECHNIQUE FOR CLOSURE OF INTERVENTRICULAR SEPTAL DEFECTS

Benson B. Roe, M.D., San Francisco, Calif.

THE TECHNICAL difficulties of precisely placing sutures in interventricular septal defects are well known to cardiac surgeons. A right ventriculotomy which does not traverse major coronary vessels often does not provide ideal exposure of the ventricular septum in the defect area, and the septal leaflet of the tricuspid valve often obscures the lower edge of the defect. Under these circumstances it is frequently awkward or impossible to place an ordinary suture needle in the ideal location and proper direction through the tissue. A large curved needle is difficult to manipulate in the limited exposure and a smaller needle may be impossible to grasp when placed through the septal edge.

An ordinary needle holder can be manipulated only by rotation on its long axis, particularly when it is introduced into a confined space. Motion of the needle it grasps is thus necessarily limited to the plane at right angles, regardless of how it is mounted or the curvature in the jaws (Fig. 1). Directing the needle in any other plane is reflected by motion of the instrument handle as a long lever. This motion is manifestly awkward or impossible inside the ventricle. Nevertheless, the desired needle direction is often in a plane parallel to, or at acute angles to, the axis of the needle holder.

To solve this difficulty, a simple curved needle hook is used as described in the accompanying diagrams (Fig. 2). It is easily handled and directed; its total size is small and does not obscure the field. Its piercing arm is sufficiently long to be easily seen, and it has no tail to snare or pierce adjacent tissues. Its only drawback is the necessity of passing double thicknesses of suture material adjacent to the needle through the septum; however, the size of this puncture hole is not significant and is doubtless smaller than some holes produced by the tearing action of misdirected needles. Furthermore, the direction

Fig. 2.—Technical steps in placing a mattress suture through the septal edge.

1, The needle is mounted with the arm of suture through the inside of the needle grasped with the handle; the short free end extends through the outside of the hook as it penetrates the tissue.

2, The outside loop is snared to draw the *a* end through.

3, With the *a* end secured, the needle tip is withdrawn and the *b* end is released from the operator's grip.

4, The other side of the mattress suture is begun with the second needle pierce.

5, The outside loop is again snared to pull through the *b* end.

6, The hook needle is withdrawn, leaving the mattress suture in place.

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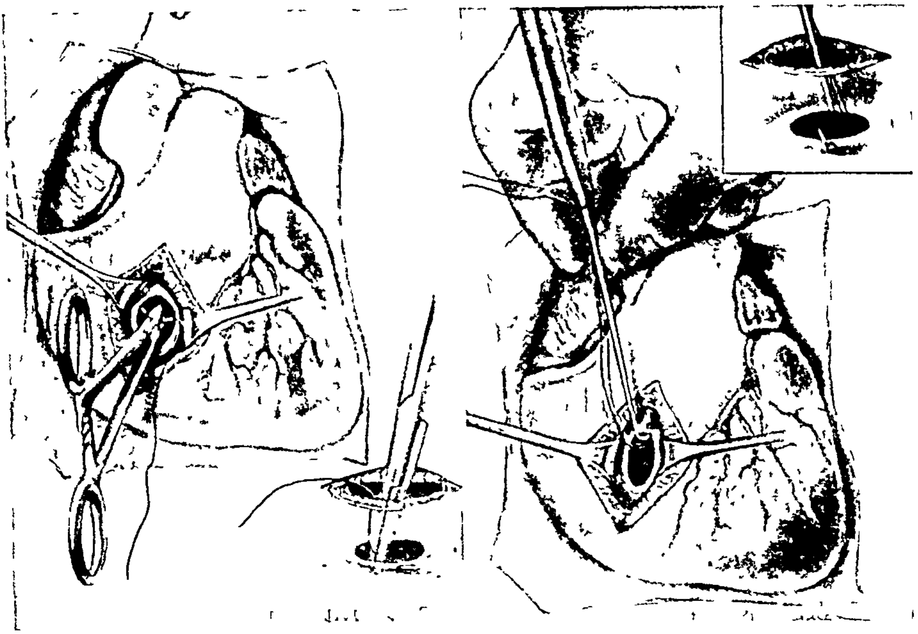


A. B.

Fig. 1—A curved needle mounted on a needle holder *(A)* cannot be directed through the septal tissue without obliquity. The hook needle *(B)*, with the point parallel to the shaft, can be drawn with a simple upward motion

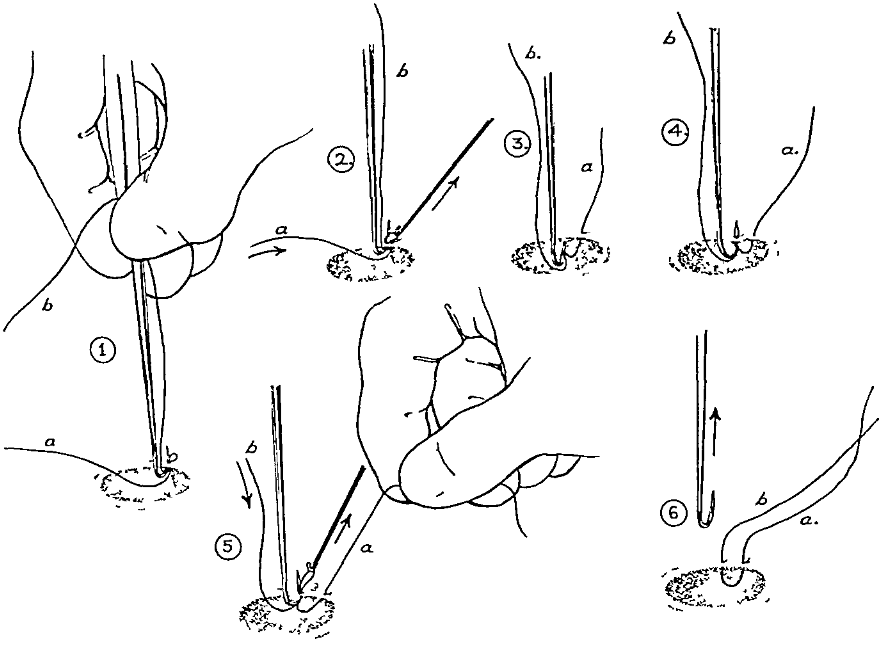
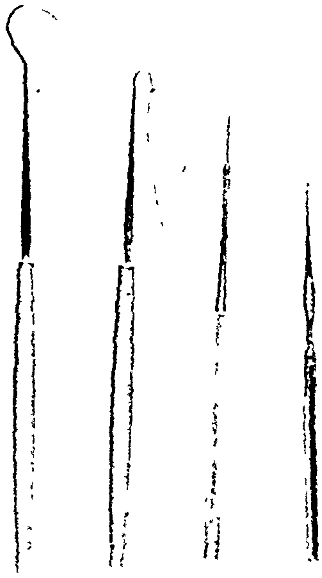


Fig. 2.—*For legend see opposite page,*



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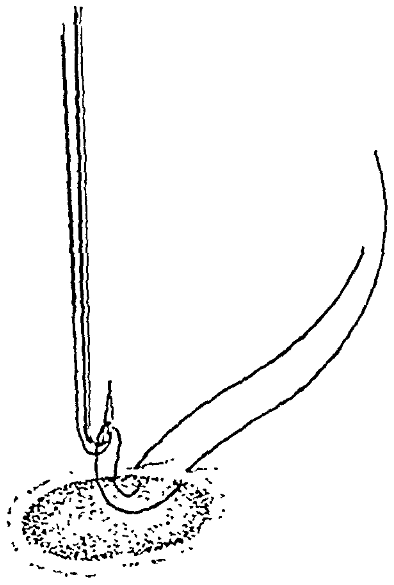

Fig. 4.

Fig. 3.—Instruments used, left to right. Tonsil needle from which hooks were adapted. Hook needle used in this technique. Dura hook for snaring suture loop of needle eye. Crotchet needle.

Fig. 4.—Result if wrong loop is snared from the needle holder in the second stage. Suture will have to be withdrawn if this occurs

Fig. 5.—Special curved hollow needle with *spool* of suture material delivered through tip. The piercing arm of this needle is a No. 22 hypodermic size. In effect, the *b* arm of the suture loop in Fig. 2 is in the shaft of the instrument, rather than floating loose.

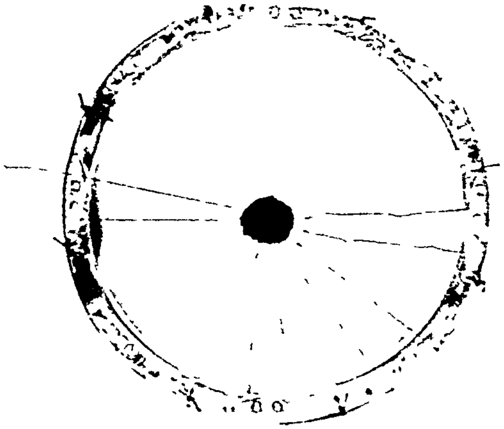

Fig. 6.—The Figure shows the suture ring with 8 clips showing sutures in place, draped over a special sheet which covers the rest of the operative field.

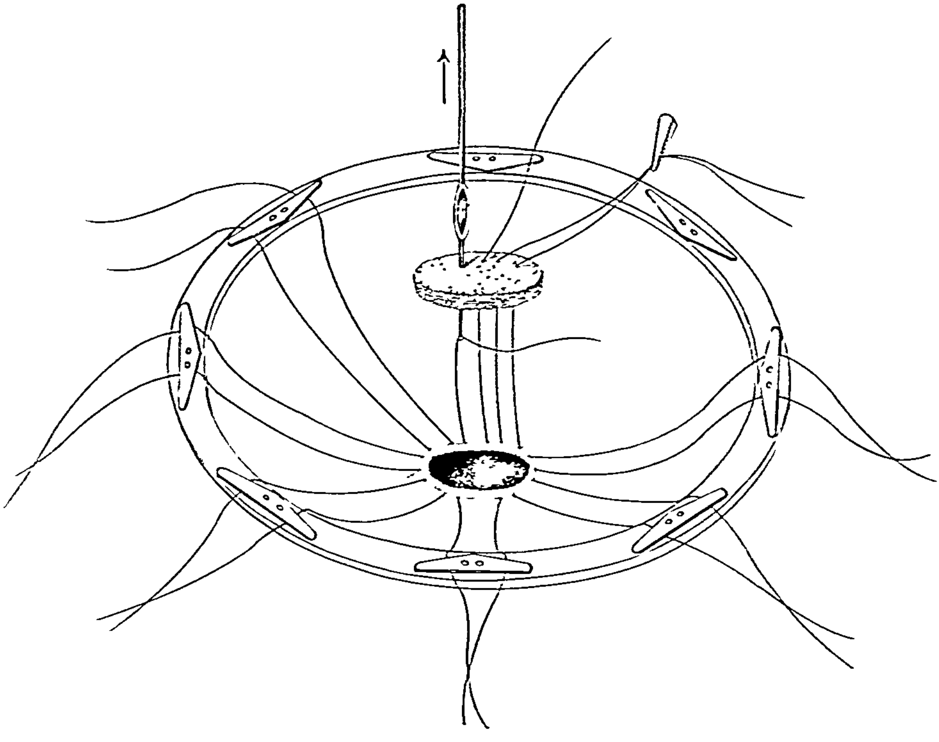

Fig. 7.—The use of the crochet hook to travel suture ends through the plastic sponge patch is demonstrated. The crochet hook penetrates the patch in the desired position and the proper suture end is looped on to it and it is withdrawn.

of tension on the suture tends to be in a straight line through the septum; a curved needle travels through this thick tissue in a circular course which must be distorted or torn when straight tension is applied.

This method of suturing can be accomplished as illustrated with a simple tonsil hook needle which has been rebent into a more suitable curve (Fig. 3). Practice is required to snare the correct side of the loop with a sharp pin hook so as not to tear the delicate septal tissue and not to have the loop left through the needle eye after both ends are through the tissue (Fig. 4). A new instrument has been developed to facilitate this maneuver and to reduce the size of the needle puncture hole. It consists of a hollow shaft and needle tip (No. 22 hypodermic needle) which carries the suture and delivers a single end of suture from a spool on the handle (Fig. 5).

The technique is rapid for several reasons: (1) the hook is easy to handle and simple to direct into the desired position; (2) both arms of the mattress suture are introduced with a single mounting in the needle, thus obviating the withdrawal of the needle holder and grasping a separate needle; (3) the absence of multiple needles around the incision and the use of a suture ring (Fig. 6) reduces the tangle in the operative field; and (4) the crochet hook facilitates bringing the sutures through the patch material with a simple straight down and up motion (Fig. 7) obviating the multiple maneuvers of mounting, grasping, and cutting 12 to 16 curved needles.

Experience with this technique in the closure of ventricular septal defects, when patches have been used, has significantly reduced the operating time during cardiotomy and largely obviated the necessity of elective cardioplegia.

SUMMARY

A simplified timesaving technique for introduction of sutures in confined areas is described. Its application for placing of mattress sutures for closure of interventricular septal defects with patches has significantly reduced operating time.

AN EFFECTIVE BLOOD HEAT EXCHANGER FOR DEEP HYPOTHERMIA IN ASSOCIATION WITH EXTRACORPOREAL CIRCULATION BUT EXCLUDING THE OXYGENATOR

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Extracorporeal circulation with deep hypothermia has made it possible to perform prolonged intracardiac operations in a bloodless field without the use of an oxygenator as shown by Drew. Deep hypothermia is therefore an alternative to the pump-oxygenator. The aim of this paper is to describe a heat exchanger which has proved effective in experiments as well as in clinical cases for the induction of deep hypothermia.

METHOD

Thirty-nine perfusions with a disc oxygenator were first performed to provide a basis for comparison. Then the method of deep hypothermia with extracorporeal circulation was tried on dogs, utilizing the same pumps, tubings, connectors, reservoirs, and filter. The disc oxygenator was replaced by a heat exchanger. In the animal experiments, a subcostal incision was made under the fourth rib on the right side. Heparin, 2 mg. per kilogram of body weight, was injected directly into the right atrium. One cannula (Bardic catheter) was introduced through the interatrial groove into the left atrium and another into the right atrium through its appendix. These two cannulas were connected with reservoirs. A metal cannula was introduced into the femoral artery in the usual fashion (Fig. 1).

The perfusion was begun by draining blood from the left atrium at a rate of 100 to 250 ml. per minute into a reservoir. The blood was then pumped through the heat exchanger and a filter into the femoral artery. After 10 to 20 minutes, the esophageal and rectal temperature reached 18° to 22° C. and the heart went into ventricular fibrillation. The left-sided perfusion was then stopped while a cannula was introduced into the main pulmonary artery through a stab wound in the right ventricular wall. Blood from the right atrium was drained into a reservoir and pumped through this tube into the pulmonary artery, oxygenated in the lungs and returned to the left atrium and to the left-sided perfusion. In other words, one pump acted for the left, one for the right ventricle. The blood was cooled or warmed in the left perfusion circuit and oxygenated by the lungs in the right circuit (Fig. 1).

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Once fibrillation occurred, the left perfusion was momentarily stopped, then the left and right perfusions were simultaneously begun at an approximate rate of 50 ml. per kilogram of body weight per minute. Within 15 to 20 minutes the esophageal temperature was brought below 10° C. Oxygen consumption is low at this low temperature and the relatively high flow loads the tissues with oxygen. Then the perfusion was stopped, the superior and inferior venae cavae as well as the aorta and the pulmonary artery were occluded. This placed the heart in hypothermic arrest, and a right ventriculotomy was performed. The right ventricle was left open for 30 minutes, then filled with glucose and the left and right perfusions started again at an approximate rate of 50 ml. per kilogram per minute. At a temperature of about 30° C. the heart spontaneously resumed its regular rhythm or was electrically shocked. The right perfusion was stopped and the right atrium and the pulmonary artery were decannulated. The left perfusion was continued for rewarming until a rectal temperature of 34° C. and an esophageal temperature of about 38° C. were reached. After decannulation, 3 mg. of protamine were administered and the wound was closed.

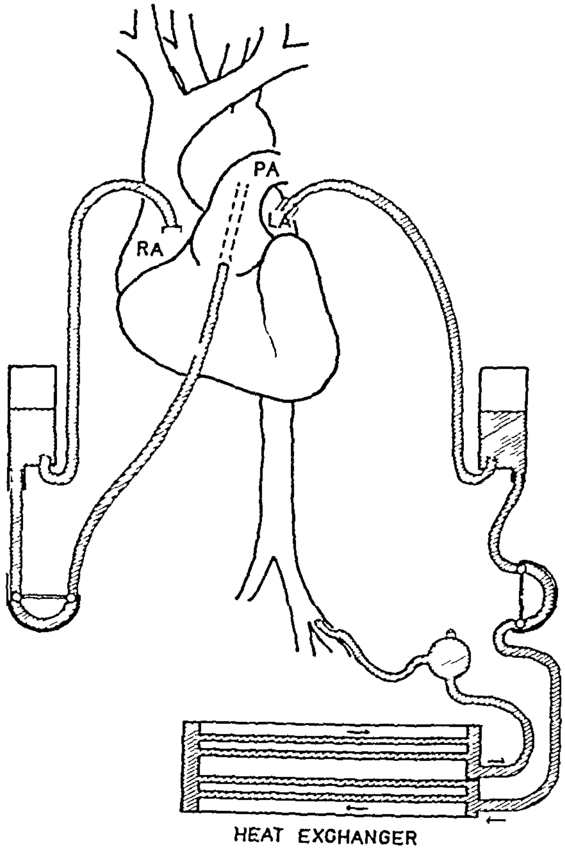

Fig. 1.—Diagram of the cannulation of left atrium, right atrium, femoral artery, and pulmonary artery for deep hypothermia. The left circuit includes the heat exchanger and the right circuit provides oxygenation in the patient's own lungs (according to Drew).

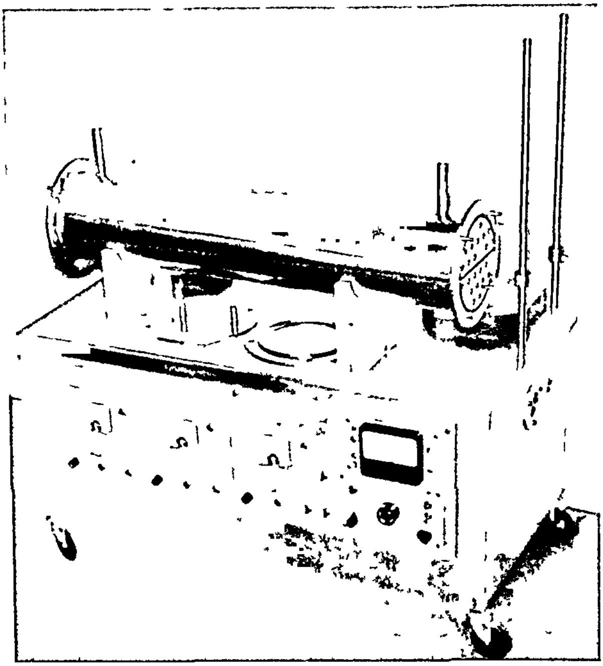

Fig 2—The heat exchanger mounted on a Mark machine with two De Bakey roller pumps The blood enters the tube in the lower part of the cylinder and comes back through the tubes in the upper part of the cylinder. The water for cooling and warming enters the upper connections

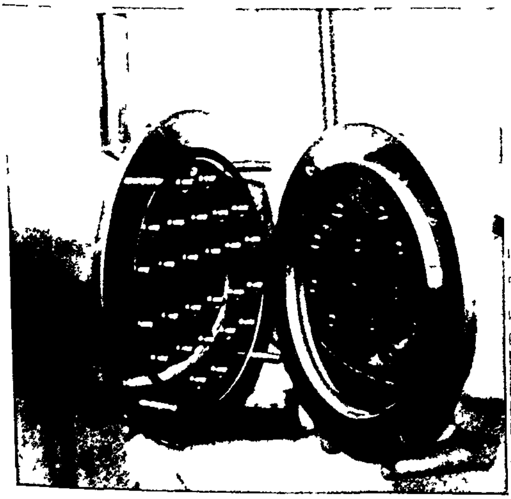

Fig 3

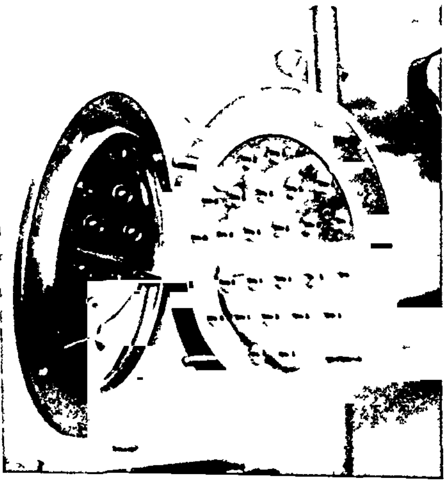

Fig 4

Fig 3—Demonstrating one end of the heat exchanger with the rod in place

Fig 4—Demonstrating the other end of the heat exchanger where the blood enters in the lower portion and leaves in the upper portion of the heat exchanger

The heat exchanger was built of stainless steel tubes mounted in a stainless steel cylinder (Figs. 2, 3 and 4). The tubes are 80 cm. long and have an internal diameter of 1 cm. thereby making mechanical cleaning easy. Into each tube a stainless steel rod of 7 mm. external diameter with rounded edges is introduced. By these measures (1) the perfusion pressure is not increased at a flow up to 3,000 ml. per minute, (2) 900 ml. less blood is needed, and (3) the cooling or warming efficiency on the thinner layer of blood is increased (Fig. 5). Through the cylinder outside the tubes, warm or cold water is circulated and the temperature thermostatically controlled by a Therm-O-Rite apparatus. For cooling water at a temperature of +2° C. and for warming water at a temperature of 41° C. at a flow of 6 L. per minute was used. A higher flow rate up to 25 liters is advised for adults. The blood leaving the heat exchanger should have a temperature of from 5° to 10° C. during the cooling and between 38° and 39.5° C. during rewarming.

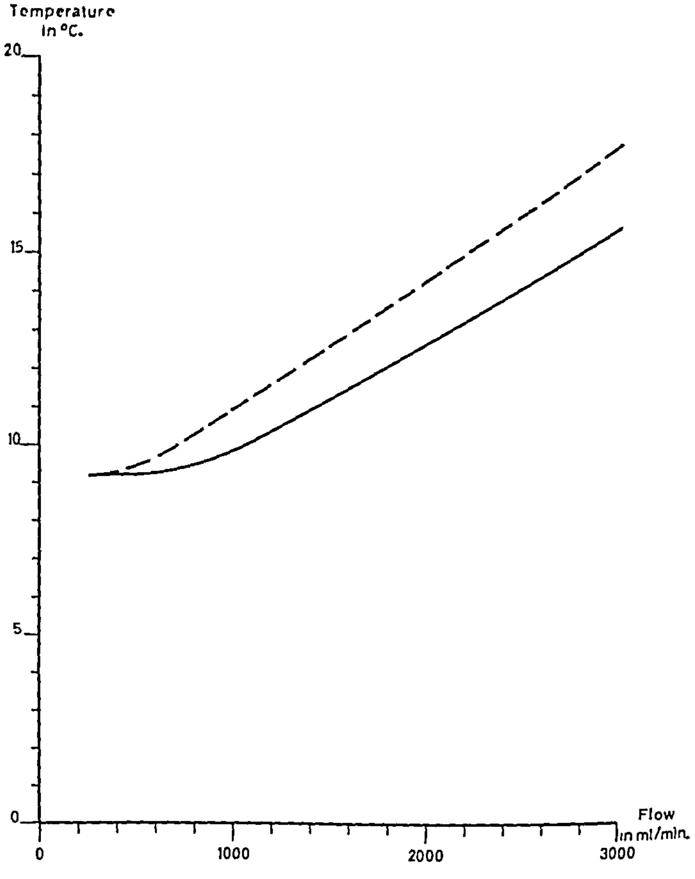

Fig. 5.—The cooling efficiency of the heat exchanger with the rods (*lower curve*) and without the rods (*upper curve*), demonstrating that at a very low flow the blood going through the heat exchanger once will have about the same temperature as the cooling fluid which during this experiment was 8° C. flowing through the heat exchanger at a rate 24 liters per minute. With a higher rate of blood flowing through the heat exchanger, the cooling efficiency was better if the rods inside the tubes were used (*lower curve*). At a flow rate of blood of 3,000 ml. per minute, the blood leaving the heat exchanger was 2° C. colder when the internal rods were used.

RESULTS

First Step of Cooling.—From experiences thus far gained, it is considered that the first step of cooling should start with a rather slow perfusion rate of about 100 c.c. per minute in small patients and up to 1,000 ml. per minute in heavier patients. In this way ventricular fibrillation will occur at an esophageal temperature between 16.5° and 25.8° C., with a temperature approximately similar in the rectum.

We have investigated the oxygen tension in the blood leaving the heat exchanger at the slowest flow rate used, i.e., 100 ml. per minute, and found that after 6 minutes of perfusion an oxygen tension of 86 mm. Hg is reached. At such a slow perfusion rate, full saturation is reached in the blood which leaves the heat exchanger long before ventricular fibrillation occurs. Data for oxygen tension, checked every minute, of blood leaving the heat exchanger are given in Fig. 6. Data of rate of cooling and the occurrence of ventricular fibrillation at different flow rates and different temperatures are summarized in Table I.

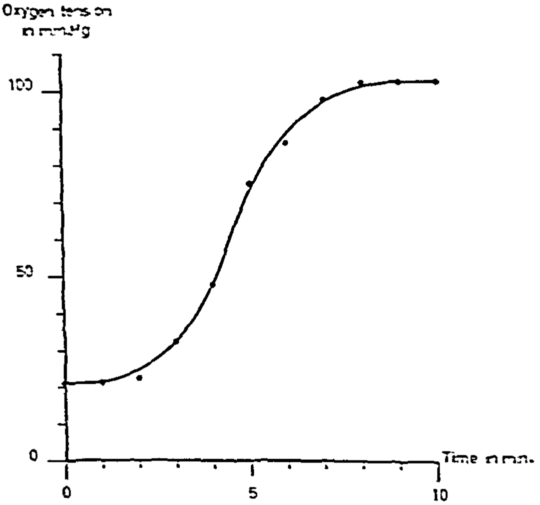

Fig. 6.—Curve showing the oxygen tension in the blood leaving the heat exchanger at a flow rate of 100 ml. per minute. Determinations were made every minute.

The Second Step of Cooling.—Once the ventricular fibrillation has started the left-sided perfusion is immediately stopped. Otherwise, there will be built up a high venous pressure during the time blood is pumped into the femoral artery but not being pumped away by the right heart.

Through a stab wound in the right ventricular wall, a Bardic catheter is put through into the pulmonary artery. It is important that the tip of the catheter be placed peripherally to the pulmonary valves. There is danger of leakage into the right ventricle in patients with high pulmonary resistance and, therefore, need for having an occlusion tape around the tip of the catheter. In cases of tight pulmonary valves in which it is difficult to introduce a Bardic catheter, a metal cannula similar to the one used in the femoral artery has been inserted. Once the catheter is in place, perfusion is started simultaneously

TABLE I. FIRST STEP OF COOLING*

	WEIGHT (KG.)	RATE OF PERFUSION (ML./MIN.)	TIME (MIN.)	TEMPERATURE (°C.)			
				ESOPHAGUS	RECTUM	IN BLOOD LEAVING THE HEAT EXCHANGER	
Dog number							
40	30	1,500	10	31.6		-10	
41	20	2,000	3	25		+10	
42	24	1,400	3	37		9·7	
43	19	500	5	23.4	28.2	9	10
44	25.5	500	12	29.5	31.2	14	11.4
45	31	500	15	31.8			
Patient number							
2	13.6	100	16	17.8	17.5	4.5	4 5
6	15.6	100-250	22	18.9	18.7	4.5	2.5
7	26.5	250	11	17.0	23.8	11	9
4	28.3	100	10	20.2	22.3	3	5
5	51.8	100-250	24	19.6	21.0	2.5	5.5
1	65	250	18	19.0	17.3	4.5	9.7
3	73.7	250	18	25.8	23.8	3.5	7.5
8	50.0	500	9	30.0	24.0	4.5	10
9	19.1	100	27	16.5	14.4	3.0	4 5
10	15.4	100	16	16.3	24.5	3.5	4.0

*Blood drained from left atrium and pumped through the heat exchanger into the femoral artery until ventricular fibrillation occurs.

on the left and right sides. The left pump is increased until a rate of around 50 ml. per kilogram of body weight is reached, which flow rate is thought to be the ideal one since very little pressure gradient over the femoral cannula is obtained. The right pump is kept at about the same speed as the left one but regulated according to the level in the reservoir draining the left atrium. Once the blood in the left reservoir is low, the right pump speed is increased, which immediately will increase the level of blood in the left reservoir. The blood thus pumped through the lungs immediately drains down into the left reservoir and is pumped through the heat exchanger back into the femoral artery.

All dog experiments and clinical experiences with perfusion rates of the second step of cooling are summarized in Table II.

The second step of cooling should be done at a much higher speed than the first step. Probably a rate of 50 ml. per kilogram of body weight is ideal. This will not cause too high a pressure gradient over the arterial cannula and will lower the temperature as quickly as possible. There has been no difficulty in keeping the same flow rate on the right- or left-sided perfusion in all cases, except those in which the pulmonary cannula has slipped out or when there has been an abnormal venous return with an intact atrial septum or a very high pulmonary resistance.

The Temperature Change During Total Arrest in Deep Hypothermia.—As the room temperature is much higher than the temperature of the patient during deep hypothermia, it is important to know the increase in temperature during the total arrest. Furthermore it is important to know if that change or increase in temperature during the total arrest was more rapid if the cooling time was short as compared with a longer cooling time. These experiments are

TABLE II. SECOND STEP OF COOLING = TOTAL PERFUSION*

	WEIGHT (KG.)	RATE OF PERFUSION (ML./MIN.)	TIME FOR RIGHT – LEFT PERFUSION (MIN.)	TOTAL TIME FOR COOLING (MIN.)	TEMPERATURE AT TOTAL ARREST (°C.)		
					ESOPHAGUS	RECTUM	IN BLOOD LEAVING THE HEAT EXCHANGER
Dog Number							
40	30	2,000	60	70	16.7		
41	20	2,000	32	35	9.5	11.4	
42	24	1,400	58	60	9.0	16.0	7.0
43	19	1,500	18	23	9.5	14.8	10.0
44	25.5	2,000	42	54	10.0	17.1	11.4
45	31	1,500	51	66	10.4	15.2	
Patient Number							
2	13.6	700	14	30	5.8	15.4	5.0
6	15.6	800	7	29	10.0	18.4	6.0
7	26.5	1,300	5	16	10.0	21.8	7.5
4	28.3	1,000	26	36	7.8	20.0	5.3
5	51.8	2,200	10	34	10.0	21.0	8.5
1	65	2,290	12	30	14.7	16.0	11.7
3	73.7	2,000	27	45	7.5	19.0	11.7
8	50	2,500	24	33	10.0	19.2	6.0
9	19.1	800	8	35	10.0	12.4	3.0
10	15.4	750	5	21	10.0	21.0	3.0

*Left perfusion with cooling = first step plus drainage of blood from right atrium and pumping that blood back through the pulmonary artery (right perfusion with oxygenation of blood in the lungs). Left and right perfusion at the same rate was continued from ventricular fibrillation until complete arrest with cardiotomy

shown in Table III, which shows that the shorter cooling time resulted in the highest temperature increase during the total arrest. The difference, however, is so small that it was considered to be without practical value. If too long a cooling time was used, the method would not be suitable for clinical use. Therefore in the clinical cases a trial was made to obtain a cooling time as short as possible.

TABLE III. THE TEMPERATURE CHANGE DURING TOTAL ARREST IN DEEP HYPOTHERMIA IN DOGS

DOG NUMBER	TOTAL TIME FOR COOLING (MIN.)	TOTAL ARREST (MIN.)	TEMPERATURE CHANGE (°C.)	
			ESOPHAGUS	RECTUM
43	23	30	-3.3	-0.4
41	35	30	-6.5	-4.6
44	54	30	+1.2	-1.9
42	60	30	-2.5	+1.5
45	66	40	-3.0	-1.2
40	70	30	-1.3	—

The temperature changes during total arrest in deep hypothermia in the patients are summarized in Table IV. From these data it can be concluded that there will always be a temperature increase both in the esophagus and in the rectum during the total arrest, increasing the metabolic needs of the patient. A period of total arrest longer than 45 minutes is not recommended for an adult and if it is evident after 40 minutes of surgery that more than 5 minutes' time is needed to complete the operation it is advised that a second short perfusion of cold blood for about 15 minutes be employed to again load the tissues with oxygen. Furthermore, the very rapid cooling, as in Case 7, in which an esophageal temperature of 10° C. was reached in 16 minutes allowed a total arrest of 44 minutes with only 4.3° C. increase in temperature in the esophagus, followed by an excellent recovery.

TABLE IV. THE TEMPERATURE CHANGE DURING TOTAL ARREST IN DEEP HYPOTHERMIA IN PATIENTS

PATIENT NUMBER	TOTAL TIME FOR COOLING (MIN.)	TOTAL ARREST (MIN.)	TEMPERATURE CHANGE (°C.)	
			ESOPHAGUS	RECTUM
7	16	44	+4.3	+1.9
6	29	38	+5.0	+2.6
2	30	70	+9.6	+4.6
1	30	25	+0.9	+2.6
5	34	21	+3.8	+0.6
4	36	49	+6.7	+2.9
3	45	47	+2.2	+1.4
8	33	27	+1.6	+2.2
9	35	50	+3.4	+8.0
10	21	41	+7.3	+2.0

Rewarming.—The experiences from rewarming of patients are summarized in Table V. From that table it is found that the shortest total rewarming time was 27 minutes in a patient of only 15 kilograms. The longest rewarming time was 135 minutes and the next longest 91 minutes in a patient weighing 73.4 kilograms. A flow of approximately 50 c.c. per kilogram of body weight was used.

TABLE V. FIRST AND SECOND STEPS OF REWARMING*

CASE NUMBER	WEIGHT (KG.)	TOTAL WARMING TIME (MIN.)	FLOW (ML.)	FIRST STEP			REGULAR RHYTHM	SECOND STEP		
				TIME (MIN.)	TEMPERATURE			TIME (MIN.)	TEMPERATURE	
					ESOPH.	RECTUM			ESOPH.	RECTUM
6	15.6	33	800	12	31.8	27.5	Sp.†	21	38.6	33.0
7	26.5	34	1,300	9	33.0	27.2	Sp.	25	38.6	34.5
2	13.6	39.5	700	10	31.2	28.8	Sp.	29.5	38.0	34.2
5	51.8	72	2,000	16	34.4	24.6	Sp.	56	38.6	34.2
1	65	75	1,900	22	34.2	23.6	Shock	53	36.0	33.4
3	73.4	91	2,000	28	33.0	23.5	Shock	63	36.7	31.0
4	28.3	94	1,000	54	38.2	28.2	Shock	40	38.0	33.0
8	50.0	135	2,000	65	37.8	27.6	Shock	70	38.2	34.0
9	19.1	32	800	13	30.6	29.2	Sp.	19	38.4	33.4
10	15.4	27	750	11	34.5	28.4	Sp.	16	38.0	34.6

*First step of rewarming: left and right = total perfusion until regular heart rhythm occurs spontaneously or after an electric shock. Second step of rewarming with only left-sided perfusion.

†Spontaneously.

Regarding the first step of rewarming when both left- and right-sided perfusions were used simultaneously—this was continued until a regular heartbeat returned, which occurred spontaneously in 5 cases and probably would have occurred in Cases 1 and 3 if we had waited until higher rectal temperatures were reached. A regular heartbeat returned spontaneously at an esophageal temperature varying between 31.2 and 34.4° C., with a rectal temperature of 24.6 up to 28.8° C. In 2 cases, the hypothermic arrested heart resumed a regular rhythm at 20° C. without an intermediate ventricular fibrillation being observed.

It is evident therefore that one may have to wait until a rectal temperature of 28.8° C. has been reached before a regular heart rhythm will return spontaneously. The shortest rewarming time to obtain a regular heartbeat was 9 minutes in Case 7. In the 4 cases in which it was necessary to shock the heart to regain regular heart rhythm only one shock, 2.5 amperes and 0.16 second, was needed in 3 cases.

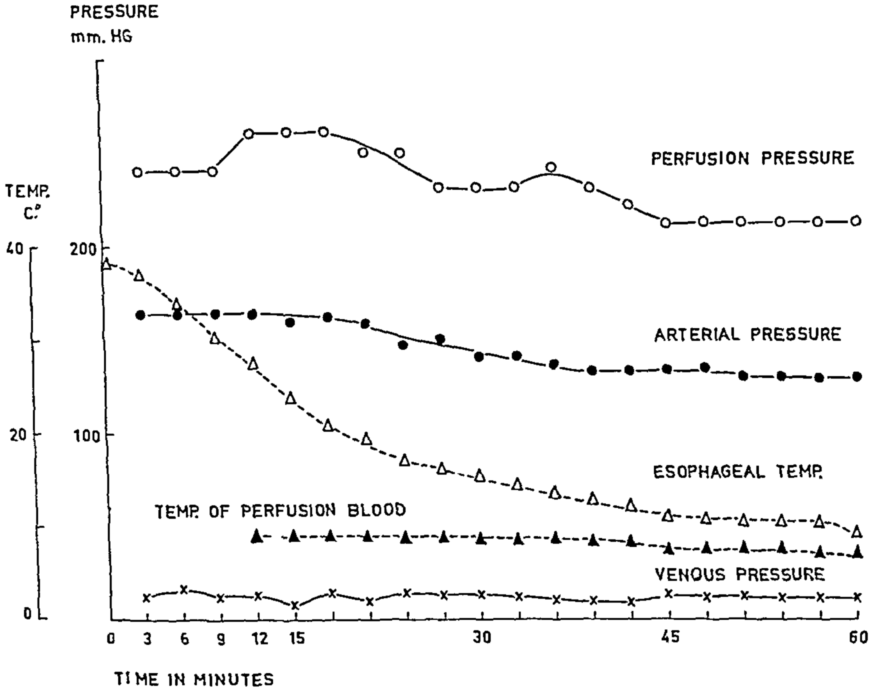

Fig. 7.—Diagram of a dog experiment under total perfusion in which it can be seen that the perfusion pressure rises during a cooling.

Once a regular heartbeat was restored, the right perfusion was immediately stopped, the cannula in the pulmonary artery and right atrium removed, and left-sided perfusion continued at the same rate. For the clinical cases we preferred to reach a rectal temperature above 34° C. before the left perfusion was stopped. Then the esophageal temperature was always above 38° C. and the patient regained consciousness rapidly after conclusion of the procedure.

In conclusion it can be said that the rewarming time has been dependent on the size of the patient and the flow of fluid through the heat exchanger. Our aim is to use a rewarming time as short as possible.

The Pressures in the Machine and in the Patient During the Perfusion (Fig 7).—If a total perfusion was carried out with a constant flow, it was found that during the cooling procedure only in the beginning there was an increased vascular resistance with increase in the pressure in the machine and an increase in the pressure gradient over the arterial cannula. This pressure gradient over the cannula tended to be somewhat lower when the temperature was below 20° C. The pressure gradient over the arterial cannula was measured in the smallest patient, weighing 13.6 kilograms in whom a cannula of 3.5 mm. was utilized. *Pressure in the machine at a flow of 700 ml. per minute* varied between 170 and 155 mm. Hg when the patient's pressure was 85 to 75 mm. Hg. In the beginning of the rewarming period, the pressure was 135 mm. Hg but rose to 175 mm. Hg in the machine with a simultaneous rise in the patient of 60 to 90 mm. Hg. Corresponding measurements in the heaviest patient, weighing 73.7 kilograms, showed the highest pressure to be 300 mm. Hg in the machine at a flow of 2,500 ml. per minute with a simultaneous pressure of 70 mm. Hg in the patient. This was an occasional value; most values were 150 mm. Hg in the machine and 80 in the patient at a flow of 2,000 ml. per minute. During rewarming, the corresponding pressures were 240 mm. Hg in the machine and 80 mm. Hg in the patient.

Hemolysis.—The data of hemolysis are summarized in Table VI. It is immediately evident that in the animal experiments a plasma hemoglobin of 19 mg. per cent at the end of perfusion is extremely low, when compared with a plasma hemoglobin of 83 mg. per cent when a pump oxygenator was used. In patients a plasma hemoglobin level of only 14.4 mg. per cent was observed. These are the only data favoring the superiority of the method of employing a heat exchanger instead of a pump oxygenator.

TABLE VI. THE HEMOLYSIS OF THE BLOOD IN MG. % PLASMA HEMOGLOBIN AFTER DEEP HYPOTHERMIA WITH EXTRACORPOREAL CIRCULATION

	TOTAL TIME OF PERFUSION (MIN.)	HEMOLYSIS BEFORE PERFUSION		AFTER END OF PERFUSION	>2 HOURS AFTER PERFUSION
		ARTERY	MACHINE		
Dog number					
40	145	0	7	26	28
41	70	0	—	28	—
42	100	6	15	8	8
43	67	0	12	16	10
44	104	0	11	17	10
Mean values	97		11	19	14
Patient number					
1	105	3	5	5	—
2	69	12	38	18	0
3	136	3	15	10	0
4	130	2	8	18	20
5	106	6	—	17.5	—
6	62	0	—	28	0
7	50	0	2	28	0
8	168	4	—	11	5
9	67	0	—	6	5
10	48	0	6	2.5	0
Mean values	94	3	12	14.4	4

Thrombocytes.—The influence of the heparin dosage on the number of thrombocytes during deep hypothermia was studied in the following way. The heparin dosage was varied from 1.5 to 3 mg. per kilogram of body weight. At a dosage of 3 mg. per kilogram of body weight, the number of thrombocytes fell from 191,000 to 90,000 at an esophageal temperature of 9.5° C. During rewarming the number of thrombocytes again increased to 224,000, still remaining at 224,000 at 2 hours after the end of perfusion. In the experiments in which 1.5 mg. heparin per kilogram of body weight was used, a fall from 161,000 to 63,000 thrombocytes at a temperature of 10.0° C. was observed. During rewarming the number of thrombocytes returned to 198,000 and 2 hours after the end of perfusion they numbered 171,000.

It can therefore be concluded that although there was a significant fall in the number of thrombocytes at low temperatures, a normal number of circulating thrombocytes was found during the rewarming process with a heparin dosage of 1.5 mg. per kilogram of body weight. A dosage of 2 mg. per kilogram of body weight was used in clinical cases, later this dose was increased to 5 mg. The values of the thrombocytes before, during, and after deep hypothermia in the clinical cases are summarized in Table VII. Although the number of thrombocytes may be as low as 34,000 at 7.8° C., the number has always been normal at the end of rewarming. After the end of the procedure, the heparin has been neutralized with protamine which has restored the bleeding and coagulation time to normal in all clinical cases in which there has been no problem with postoperative bleeding.

TABLE VII. THE NUMBER OF THROMBOCYTES IN THOUSANDS BEFORE, DURING, AND AFTER DEEP HYPOTHERMIA IN CLINICAL CASES

CASE NUMBER	BEFORE PERFUSION	AT THE LOWEST TEMPERATURE		AT END OF REWARMING	2 HOURS AFTER PERFUSIONS
		TEMP.	THROMBOCYTES		
1	131	14.7	128	130	116
2	105	5.8	47	—	85
3	162	7.5	81	—	155
4	204	7.8	34	124	176
5	62	10.0	67	136	159
6	230	10.0	63	—	157
7	189	10.0	88	210	189
8	212	10.0	75	170	113
9	149	10.0	54	129	—
10	249	—	—	196	225
Mean values	169	9.5	71	109.5	137.5

The Red Blood Corpuscles (Table VIII).—The red blood corpuscles were counted before, during the cooling period, during the rewarming period, after the end of perfusion, and 2 hours after the perfusion. There were no significant changes either in the animal experiments or in human beings.

The Hematocrit.—There was no significant change in the hematocrit during the performance of deep hypothermia. In the only case in which a drop from 74 down to 47 per cent was noted was in a very cyanotic patient with tetralogy of Fallot.

The Hemoglobin.—No significant change in hemoglobin concentration was encountered during deep hypothermia.

The White Blood Corpuscles.—The white blood corpuscles, however, showed a significant decrease during the lowest temperature at deep hypothermia. At the end of the rewarming period, however, the number of white blood corpuscles

TABLE VIII. VALUES BEFORE, DURING, AND AFTER DEEP HYPOTHERMIA

	MEAN VALUES			
	BEFORE	AT LOWEST TEMP.	AFTER	2 HOURS AFTER
Red blood corpuscles (in millions)				
Patients	5.2	4.8	4.8	4.7
Dogs	5	5.7	5.7	—
Hematocrit (%)				
Patients	46.1	43.2	43.4	43.8
Dogs	48.5	51.2	50	55
Hemoglobin (%)				
Patients	89.3	81.7	86.1	87.8
Dogs	103.2	106.8	106.4	119
White blood corpuscles (in thousands)				
Patients	7.456	4.889	11.414	13.500
Dogs	10.125	3.425	4.031	14.600

were at about the same level as before the perfusion and 2 hours later a significant increase in the number of white blood corpuscles had occurred. These experiences are summarized in Table VIII.

The Acid Base Balance During Deep Hypothermia (Table IX).—The oxygen tension increased during the cooling as the oxygen requirement of the body decreased and it was highest before the arrest. After the arrest there was usually some oxygen debt that had to be paid before normal oxygen tension was reached again. At the end of the rewarming there was always an oxygen tension significantly above the normal. Two hours after the completion of the operation the oxygen tension was normal in all cases.

TABLE IX. THE CHANGES IN pO_2, pCO_2, pH, AND HCO_3 DURING AND AFTER DEEP HYPOTHERIMA

	BEFORE	AT LOWEST TEMPERATURE		AT END OF REWARMING	2 HOURS AFTER
		BEFORE ARREST	AFTER ARREST		
pO_2	88	162.5	82.6	115.6	97.1
pCO_2	36.2	37.5	39.4	29.3	32.8
pH	7.47	7.42	7.35	7.49	7.42
HCO_3	25.5	23.2	20.5	21.9	21.8

The carbon dioxide tension hsowed some elevation at the end of the arrest, but all values were within normal limits during the hypothermia.

The pH showed a tendency to alkalosis during the cooling period when the body was loaded with oxygen. At the end of rewarming and 2 hours after completion of the operation there was a normal pH in all cases but 1, Case 4. In that case, a pH of 7.10 was explained by a very poor perfusion due to an abnormal venous return of the right pulmonary veins into the right atrium with an intact atrial septum. As the methods for determination of pH and pCO_2 under deep hypothermia are not accurate, the conclusions are drawn on the values obtained after rewarming.

The Standard Bicarbonate.—There was a slight decrease in standard bicarbonate during the long period of arrest. Two hours after the end of operation there was always a normal standard bicarbonate in all cases except Case 4, in whom an extreme metabolic acidosis occurred due to an intact atrial septum with abnormal venous return. This has been one of the most important reasons for favoring deep hypothermia with extracorporeal circulation to the use of an oxygenator. With the latter, after a long perfusion and cardiac arrest, there will be some cases of metabolic acidosis due to the perfusion per se. A metabolic acidosis has not been observed in deep hypothermia with a cooling down to 10° C. and with a flow during the cooling period of approximately 50 c.c. per kilogram of body weight.

Oxygen Consumption (Table X).—The total oxygen consumption is naturally small at the low temperatures and from the data so far obtained it does not seem to be worthwhile going below a temperature of 10° C. in the esophagus. Some examples of the oxygen content during the cooling period are summarized in Table X. Although at an esophageal temperature of 20° C. the color of blood in the line to the femoral artery and the pulmonary artery are about the same, it is necessary to lower the temperature to 10° C. before the body is loaded sufficiently with oxygen to withstand a circulatory arrest of 45 minutes.

TABLE X. THE OXYGEN CONSUMPTION IN MAN DURING DEEP HYPOTHERMIA*

PATIENT'S WEIGHT (KG.)	TEMPERATURE (°C.)	VOLUME PER CENT O_2		TOTAL OXYGEN CONSUMPTION (ML./MIN.)
		ARTERY	VEIN	
26.5	17	18.1	15.2	32.3
	11	18.4	17.95	5.5
	10	18.6	18.45	1.8
50	19	21.1	19.8	32
	15	21.6	21.3	7.5
	12.5	21.8	21.7	2.5
	10.2	22.15	22.10	1.25
19.6	12	17.9	17.5	6.8
	10	19.8	19.7	0.8
15.4	13.5	17.55	16.8	5.6
	10.5	18.88	18.48	3

*Measured by the difference in vol. % O_2 in blood from the cannula in the femoral artery and from the superior vena cava during total body perfusion at a known flow.

DISCUSSION

A heat exchanger for deep hypothermia is presented. The advantages of deep hypothermia with extracorporeal circulation without an oxygenator follow.

1. There is less blood trauma and less hemolysis.

2. The oxygenation in the patients' own lungs is better than in any oxygenator. No postoperative metabolic acidosis has occurred, therefore, unless there has been a very poor perfusion due to technical faults or anatomic variations, or cardiac standstill before the cooling period could begin.

3. During circulatory arrest in deep hypothermia, the myocardium is better protected than during an anoxic or potassium arrest. In the animal experiments, less incidence of tricuspid insufficiency, as a result of myocardial

impairment, was found after arrest at low temperature when compared with other types of cardiac arrest, which is especially important in cases of aortic valvular disease.

4. The surgical procedure is significantly facilitated and can be completed in a flaccid heart without any blood returning through the bronchial circulation.

5. The safety margin is increased. In case something goes wrong or the catheter slips out, the circulation can be completely arrested and there is enough time at the low temperature to correct the fault. In 1 patient, it was necessary to exchange the catheter draining the right atrium for a larger one when it was found that a much higher flow in the right circulation was needed than in the left due to abnormal return of pulmonary veins from the right lung with intact atrial septum.

6. There is better blood volume control, as a closed system is used, and there is no coronary perfusion and no loss of blood through the coronary suction system.

7. Cardiac arrest can be prolonged. A cardiac arrest of 45 minutes will not impair the myocardium and if a longer cardiac arrest is needed it is necessary only to replace the catheter and to perform a second perfusion with cold blood for 15 minutes to allow a second occlusion time long enough to complete the operation. The longest period of complete occlusion with success has been 47 minutes. In 1 patient, 70 minutes were necessary which caused brain damage. Therefore the maximum time for occlusion should be between 45 and 50 minutes There seems to be no advantage to lowering the temperature still further as the accident of brain damage occurred after 70 minutes of occlusion at 5.8° C.

In the first series of 10 clinical cases, 6 patients survived the operation. Three died of brain damage (Table XI).

The patients accepted have had ventricular septal defect, cyanotic tetralogy of Fallot, septum primum defect, and infundibular stenosis. The fourth patient who died had ventricular septal defect + infundibular stenosis + valvular stenosis + abnormal venous return from the right lung with intact atrial septum. It was not possible in his case to diminish the pressure in the right ventricle to more than 80 mm. Hg, as the stricture in the main pulmonary artery, peripheral to the valvular stenosis, was 2 cm. long and there were further multiple strictures in the smaller pulmonary arteries. The patient was considered inoperable. The method has not been used for ordinary cases of atrial septum secundum defects with or without abnormal venous return. These patients are operated upon under surface cooling at a temperature of 30° C.

The disadvantages of the use of deep hypothermia without an oxygenator in the extracorporeal circulation follow.

1. There is a time limit of 45 minutes of the circulatory arrest in adult patients.

2. Brain damage has been encountered in 3 children. I believe this brain damage is caused by a thrombus formation of aggregated thrombocytes and

TABLE XI. THE COMPLICATIONS ENCOUNTERED IN THE FIRST CLINICAL CASES UNDERGOING OPEN-HEART SURGERY WITH DEEP HYPOTHERMIA UTILIZING EXTRACORPOREAL CIRCULATION WITH HEAT EXCHANGER

CASE NUMBER	DIAGNOSIS	ESOPHAGEAL TEMPERATURE AT ARRIVAL (°C.)	TIME OF CIRCULATORY ARREST (MIN.)	COMPLICATION	RESULT
1	IS,* reoperation	14.7	25	0	Survival
2	Tetralogy of Fallot	5.8	70	Block + brain damage + wound infection	Died of brain damage
3	IS + pulmonary stenosis + ASD†	7.5	47.5	0	Survival
4	VSD‡ + IS + pulmonary valvular stenosis + multiple peripheral pulmonary stenosis + abnormal venous return	7.8	49		Died (inoperable)
5	ASD (secundum) reoperation	10.0	21	0	Survival
6	Total abnormal venous return + ASD (secundum)	10.0	38	0	Survival
7	VSD	10.0	44	Block + brain damage	Survival
8	Ostium primum defect, reoperation	10.2	27	Block + pulmonary edema	Survival
9	Tetralogy of Fallot	10.0	50	Block	Died of brain damage
10	Ostium primum with cleft mitral valve	10.0	41	Brain damage	Died of brain damage

*IS = Infundibular stenosis.
†ASD = Atrial septal defect.
‡VSD = Ventricular septal defect.

white blood corpuscles, which largely disappear from the circulation at a low temperature. During the rewarming, the aggregated thrombocytes and white blood corpuscles return to the circulation and may have occluded the circulation in certain areas in the brain for some time, with a focal necrosis as a result. At the present time, I consider the method contraindicated for children. We have not been able to prevent this thrombocyte agglutination by increased heparin dose (5 mg. per kilogram) or by dilution of blood with low molecular macrode.

3. The method of using two parallel pump systems is much more difficult to handle than an ordinary pump-oxygenator with a heat exchanger.

4. The method is considerably more time consuming.

SUMMARY

Deep hypothermia with extracorporeal cooling without an oxygenator, according to Drew, has been used in 17 clinical cases and compared with the pump-oxygenator system. After this comparison, the original deep hypothermia method has been abandoned.

The ordinary pump-oxygenator (with the spinning disc oxygenator) is preferred at normal temperature in most cases, but combined with deep hypothermia in aortic valvular disease to protect the myocardium and permit longer perfusions. In children, deep hypothermia is considered contraindicated due to the risk of brain damage. Therefore, in children, the myocardium is protected by local hypothermia, achieved by surrounding the heart with plastic bags with ice* or by isolated coronary perfusion with cold blood.

REFERENCES

Drew, C. E., Keen, G., and Benazon, D. B.: Profound Hypothermia, Lancet 745-747, 1959.
Drew, C. E., and Anderson, I. M.: Profound Hypothermia in Cardiac Surgery. Report of Three Cases, Lancet 748-750, 1959.

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*After acetylcholine arrest.

STUDIES WITH A CELLULOSE MEMBRANE OXYGENATOR

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INTRODUCTION

THE DIFFUSION of small molecules and ions from one fluid to another through a semipermeable membrane and its clinical utility in therapeutic hemodialysis is now amply documented. However, the practicality of gas transfer under similar conditions has not been generally appreciated and its clinical value has, therefore, not been fully studied. Many observers have commented on the partial oxygenation of blood during the hemodialysis of cyanotic patients.

This capability of the dialyzer to transfer respiratory gases to and from blood, combined with its action as an electrolyte stabilizer and as an excellent heat exchanger, would appear to be valuable in a number of diseases and clinical situations. With this in mind, an experimental oxygenator and carbon dioxide exchanger,* patterned after the parallel-flow, straight tube hemodialyzer[1-3] was designed and constructed by Dr. Arthur E. MacNeill to determine the performance of this design with respect to respiratory gas transfer.

THE EXPERIMENTAL OXYGENATOR

The apparatus (Fig. 1) consists of 40 flat tubes of regenerated cellulose† about 0.0015 in. wall thickness when wet, arranged in parallel with interposed nylon screens of slightly greater width. The blood film is held to approximately 0.018 cm. thick in each tube. The tubes connect to a common channel at each end of the apparatus by means of uniquely designed Teflon inserts. The transparent Plexiglas case enables the investigator to observe the blood-filled cellulose tubes and the flow of the gas transferring dialyzing bath. The unit contains 3 square meters of membrane area and is designed for blood flow rates of 1,200 c.c. per minute. The blood pathways contain a total of 280 c.c. of blood for each 3 square meters of area.

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*(MacNeill Model XII-B-40-36.)

†Visking "No-Jax" Sausage Casing (36/32 in. size, 0.0008 in. dry thickness).

A dialyzing bath solution (Table I) is equilibrated with an oxygen-carbon dioxide atmosphere by spraying and agitating it with an $O_2 : CO_2$ mixture (95.5) flowing at the rate of 3 to 5 liters per minute. The container of this bath is adequately vented to allow the escape of the carbon dioxide into the atmosphere, thus maintaining physiologic levels of carbon dioxide and providing about 2 vol. per cent of oxygen dialyzing fluid with its dissolved gases to be propelled crosswise to the long axis of the cellulose tubes through the mesh of the nylon screens at a rate of 40 to 50 liters per minute by a centrifugal pump (Fig. 2).

The blood pumps[4] used in these experiments are atraumatic pumps also designed by Dr. MacNeill. Their gentleness toward blood cellular elements

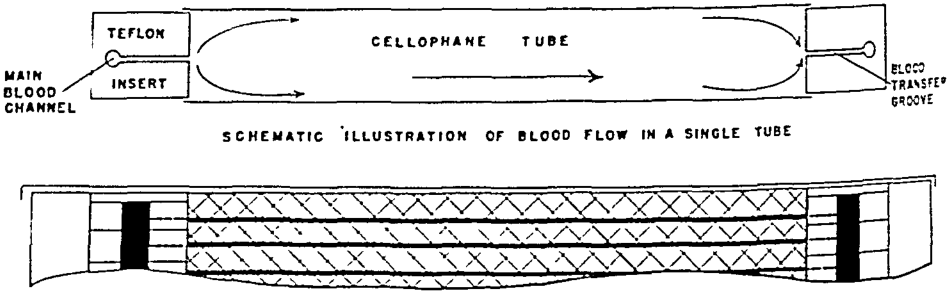

Fig. 1.—Diagrammatic representation of longitudinal cutaway side view of the interior of the oxygenator.

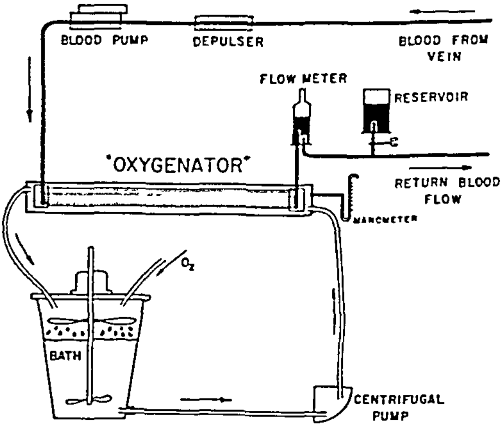

Fig. 2.—Diagrammatic representation of the bath and blood circuit and the manner in which the dialyzing solution is saturated with oxygen.

TABLE I. COMPOSITION OF THE DIALYZING BATH

	mEq./L.	MG. %
Sodium	140	
Potassium	4.5	
Calcium	4.5	
Magnesium	1.0	
Chlorine	120	
HCO_3	27.0	
Glucose		100

has been demonstrated on several occasions in patients dialyzed for renal shutdown or intoxications due to various poisons.[5] Plasma hemoglobin determinations during such clinical procedures showed a slow increase from less than 1.8 mg. per cent to a maximum of 6.5 mg. per cent in 8 hours.

PROCEDURES

I. *Oxygenation.*—Vein-to-vein and vein-to-artery perfusions (the latter requiring 2 blood pumps) at different rates of flow were performed on 16 mongrel dogs weighing from 10 to 25 Kg. (Fig. 2). The dogs were anesthetized with 1 c.c. per pound of body weight of a 2.5 per cent sodium pentobarbital solution and maintained on a respirator. Heparin, at 1.5 mg. per kilogram of body weight and 15 mg. per 500 c.c. of priming blood, was administered just before cannulization. In vein-to-vein perfusions, the blood was drawn from the inferior vena cava via a cannula inserted through one femoral vein. Blood was returned into the external jugular vein. In vein-to-artery perfusions, blood was drawn from both venae cavae by cannulas threaded through the right arterial appendage following a right thoracotomy, and returned into the right common carotid artery. Blood samples were drawn from the Tygon blood tubes before and after passing through the oxygenator. The oxygen and carbon dioxide content was determined by a method of Van Slyke.[6] Recirculation of blood was utilized in some of these perfusions to determine the rate of oxygen transfer at higher saturation levels. Two to four samples at various flow rates were taken during each perfusion. The amount of oxygen delivered per square meter of membrane used per minute was computed as follows:

$$\frac{\text{A-V diff. (vol. \%)} \times \dfrac{\text{flow rate (c.c./min.)}}{100}}{\text{Membrane area used (M.}^2\text{)}}.$$

RESULTS

I. *Oxygenation.*—The amount of oxygen picked up by a unit of blood in one pass through the oxygenator is dependent on the length of time the blood is in contact with the solution-bathed membranes and, therefore, was generally higher at the low flow rates. However, the total amount of oxygen delivered per square meter of cellulose membrane was greater at higher flow rates as indicated in the scattergram (Fig. 3). This apparatus was designed for 1,200 c.c. per minute of blood flow. Therefore, in the low ranges of flow from 100 to 500 c.c. per minute, all the cellulose tubes may not have had equal flows although they remained open. Oxygen transferred at both low and high saturation levels is illustrated in Fig. 4. The total amount of oxygen transferred through one square meter of cellulose per minute (Table II) averaged 5.4 c.c. Preliminary results, not included in the table, were inconsistent in the first perfusion studies before the numerous factors influencing gas exchange were properly controlled.

Carbon dioxide determinations on the same blood samples showed varying amounts transferred between blood and bath solution to maintain normal blood levels. The facility with which these dialyzing membranes allow the transfer of carbon dioxide is of great significance.

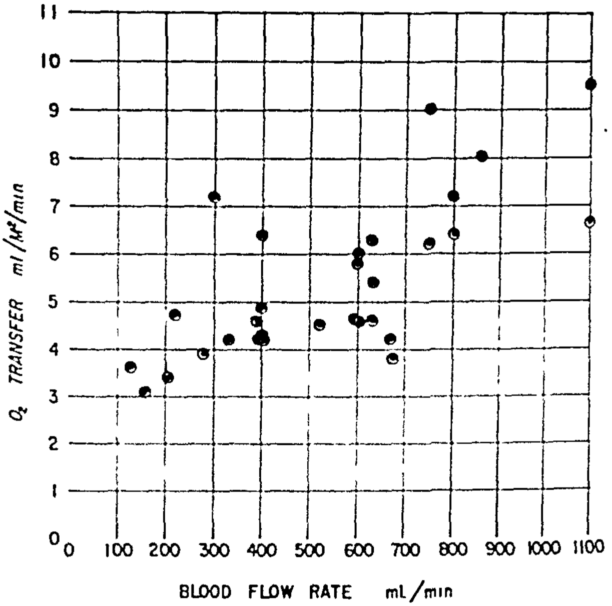

Fig. 3.—Scattergram illustrating oxygen transfer at various rates of blood flow.

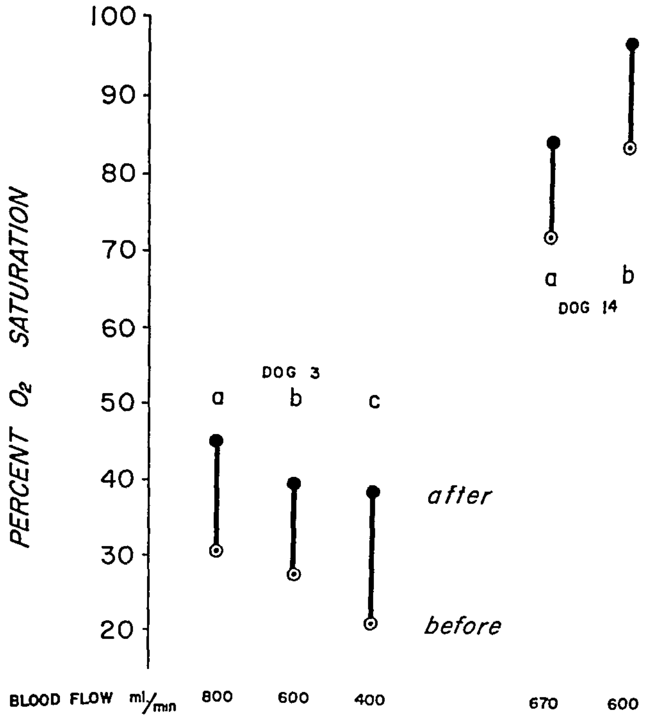

Fig. 4.—Comparison of oxygen transfer through the cellulose membrane oxygenator at both low and high oxygen saturation levels.

TABLE II. PERFUSION RESULTS AFTER ONE PASS THROUGH OXYGENATOR WITH CALCULATION OF OXYGEN TRANSFER PER SQUARE METER OF CELLULOSE MEMBRANE

DOG	RUN	FLOW RATE OF BLOOD (ML./MIN.)	BLOOD O_2 INCREASE VOL. %	O_2 TRANSFERRED (ML./M.^{2}/MIN.)
3	a	800	2.7	7.2
	b	600	2.3	4.6
	c	400	3.2	4.2
4	c	400	4.3	4.3
	d	600	2.9	5.8
5	a	400	4.8	6.4
	c	400	3.2	4.2
6	b	631	2.6	5.4
7	a	390	3.8	4.6
8	a	300	2.4*	7.2
	b	750	1.2*	9.0
9	a	675	1.7	3.8
	b	160	5.9	3.1
10	b	1,100	2.6	9.5
	c	1,100	1.8	6.6
11	a	400	3.7	4.9
	b	220	6.5	4.7
12	a	600	3.0	6.0
	b	280	4.2	3.9
	c	130	8.3	3.6
13	b	206	5.0	3.4
	c	333	3.8	4.2
14	a	670	2.1	4.2
	b	600	2.3	4.6
	c	630	2.0	4.6
15	a	750	2.5	6.2
	b	860	2.8	8.0
16	a	520	2.6	4.5
	b	630	3.0	6.3
	c	800	2.4	6.4

*Only 1 square meter of cellulose membrane was used. In remainder of runs, 3 square meters of cellulose membrane were used.

DISCUSSION

Oxygenation of the Total Circulation.—The various heart-lung machines currently used today have been designed solely for the purpose of oxygenation and carbon dioxide extraction. Except for a heat exchanger[7] which only recently has been added to some circuits for temperature regulation, no other reliable measures have been devised to prevent or correct some of the more important problems accompanying the use of these oxygenators. The most serious of these problems are electrolyte and pH abnormalities. It would seem logical, then, to seek an oxygenator that will not only deliver oxygen and extract carbon dioxide but will also maintain normal chemical and metabolic equilibrium during cardiopulmonary bypass. Similarly, anesthetic solutions, particularly Anectine and the barbiturates, might be administered through such an apparatus to maintain proper concentrations in the blood.

This experimental dialyzer-oxygenator can be expected to perform all of these useful functions. In addition, hemolysis is negligible because of the quality of the blood pumps used and because recirculation is not essential except for priming purposes. (The 3 square meter unit alone primes with 280 c.c. of blood.)

With respect to respiratory gas exchange, these perfusion studies have indicated that a dialyzer-oxygenator, built with a total area of 12 square meters of cellulose membrane, should be capable of maintaining adequate respiratory gas exchange for a child up to 10 to 15 kilograms in weight. Because it is known that the oxygen requirements decrease with lower temperatures,[8] such apparatus might be used on larger patients when combined with hypothermia. Furthermore, the maintenance of normal blood chemistry, carbon dioxide levels, pH, and proper dextrose levels may enable the subject to tolerate a greater degree of tissue hypoxia or incomplete oxygenation. Investigative studies are now being carried out with this problem in mind.

One problem which has yet to be investigated is the possibility that an oxygenating surface of 12 square meters of cellulose may be too large a dialyzing area for a child. Under such circumstances, essential trace substances might be extracted from the child's blood, with adverse results; or adsorption of either diffusible or nondiffusible substances to the extensive membrane surface may occur, leading to similar consequences. These possibilities should be investigated carefully before clinical trials of such large area dialyzer-oxygenators are attempted, as clinical experience with dialyzing membranes has not exceeded 25,000 square centimeters to date.

Oxygenation of the Partial Circulation.—Decompression by phlebotomy in addition to digitalization and other resuscitative measures in the emergency management of acute heart failure is a time-recognized procedure. Recently, shunting of blood from vein to artery, utilizing a pumping system, alone or in combination with a portable oxygenator, for the same purpose, has been reported[9] with promising results. A version of our experimental oxygenator might be similarly employed with the advantages of combined partial oxygenation, dialysis, temperature regulation, and ultra-filtration. There would be few contraindications to prolonged or repeated perfusions with the use of this unit. Use of this equipment as an aid in the emergency management of acute (temporary) pulmonary insufficiency such as occurs following pneumonectomy, in patients with borderline pulmonary function, in infiltrating parenchymal disease, pulmonary edema, emphysema, and acute laryngo-tracheo-bronchitis of infants, can also be contemplated.

SUMMARY AND CONCLUSIONS

Perfusion studies on mongrel dogs have been performed to determine the capabilities of a special parallel flow straight tube hemodialyzer as an oxygenator and carbon dioxide extractor.

The oxygenator tests have shown that 5.4 c.c. of oxygen can be transferred from an oxygen-saturated dialyzing bath solution to blood per square meter of cellulose surface per minute, and that a unit containing 12 square meters of membrane area should be capable of supplying the entire oxygen requirements of a child up to 10 to 15 kilograms in weight.

Its use in the emergency management of cardiac failure and acute (temporary) pulmonary insufficiency is postulated, based on performances demonstrated in these laboratory studies.

REFERENCES

1. MacNeill, A. E.: Synthetic Organ Mechanisms—A Challenge to the Instrument Designer, Proc. Instrument Soc. America, vol. VIII, 1953 (Paper No. 53-19-2).
2. MacNeill, A. E.: Therapeutic Instrumentation—Blood Dialyzers, Blood Pumps and Blood Flowmeters—for Bedside Therapy, Proc. Instrument Soc. America, vol. XI, 1956 (Paper No. 56-36-4-3).
3. MacNeill, A. E., Doyle, J. E., Anthone, R., and Anthone, S.: Technique With a Parallel Flow, Straight Tube Blood Dialyzer, New York State J. M. (In press.)
4. Doyle, J. E., MacNeill, A. E., Anthone, R., and Anthone, S.: Clinical Applications of a New Blood Pump, Circulation 14: 929, 1956.
5. Doyle, J. E., Anthone, R., Anthone, S., and MacNeill, A. E.: Treatment of Renal Failure With a Parallel Flow, Straight Tube Dialyzer, New York State J. M. (In press.)
6. Van Slyke, D. D., and Neill, J. M.: The Determination of Gases and Other Solutions by Vacuum Extraction and Manometric Measurements, J. Biol. Chem. 61: 523, 1942.
7. Brown, I. W., Jr., Smith, W. W., and Emmens, W. O.: An Efficient Blood Heat Exchanger for Use With Extracorporeal Circulation, Surgery 44: 372, 1958.
8. Bigelow, W. C., Lindsay, W. K., and Greenwood, W. F.: Hypothermia, Ann. Surg. 132: 849, 1950.
9. Creech, O., Jr., Krementz, E. T., Ryan, R. F., and Winblad, J. N.: Chemotherapy of Cancer: Regional Perfusion Utilizing an Extracorporeal Circuit, Ann. Surg. 148: 616, 1958.

VARIATIONS OF THE THROMBIN TIME IN CERTAIN PATIENTS UNDERGOING OPEN-HEART SURGERY: DISCUSSION OF ITS PROGNOSTIC SIGNIFICANCE

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Fibrinolysis and the appearance of an anticoagulant as measured by the thrombin time were reported by us to be two major clotting derangements which may occur during cardiac surgery with the use of a pump-oxygenator.[1] It was also noted that the presence of the anticoagulant(s) was most readily demonstrable when cardiovascular difficulties were encountered during the operative procedure or when such complications developed relatively shortly after surgery. Since that time special attention has been given to changes in thrombin time in patients undergoing cardiac surgery combining, in most instances, a pump-oxygenator with hypothermia. As a result of these observations it is considered that serial determinations of the thrombin time may be of prognostic value. Marked elevation of the thrombin time was frequently observed before a clinical manifestation of cardiovascular dysfunction occurred, and it was also observed that an elevated thrombin time before surgery coincided with a higher surgical risk. It is, therefore, believed that a marked increase in the thrombin time may reflect a disadvantageous alteration in the systemic response of the cardiac patient to surgical stress. The main emphasis of this paper is to demonstrate the possibility that there exists a relationship between the fluctuations in the clotting system as measured by the thrombin time and the development of cardiovascular complications, such as: total or partial heart block, auricular or ventricular fibrillation, severe drop in blood pressure, and reversible cardiac arrest.

The data presented are based on observations on 27 unselected patients undergoing open-heart surgery. The thrombin times were measured as indicated earlier.[1] Our original goal was to study fibrinolysis and some of the essential findings have been reported previously. A rather unexpected by-product of the study was the gross abnormalities of the thrombin time observed under these circumstances which initiated further investigation. Fig. 1 illustrates the results. It shows the mean thrombin time of these patients at various

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intervals before and during surgery. The intervals were: (a) control, either before induction of anesthesia or the day before operation; (b) after induction of anesthesia; (c) immediately after extracorporeal circulation and protaminization; (d) approximately 30 minutes after protaminization; and (e) approximately 1 hour after protaminization, and, if indicated, at successive intervals. The normal thrombin time is about 12 seconds, as represented by the dotted line in Fig. 1. The numerals below the histograms indicate the number of patients from whom the average values were obtained. The set of histograms on the bottom of the figure shows the serial thrombin times for all patients surviving the procedures. It can be seen that all their thrombin times are definitely longer than normal. If, however, the survivors are separated in two groups, one consisting of patients exhibiting no particular cardiovascular disturbances during and after the procedure, and the other consisting of those who developed dysfunction during the operation or immediately thereafter, then it becomes apparent that the patients who developed transitory circulatory dysfunctions are the ones responsible for the rise in the mean serial thrombin times of all survivors. This is indicated by the second and third set of histograms on the bottom of the figure.

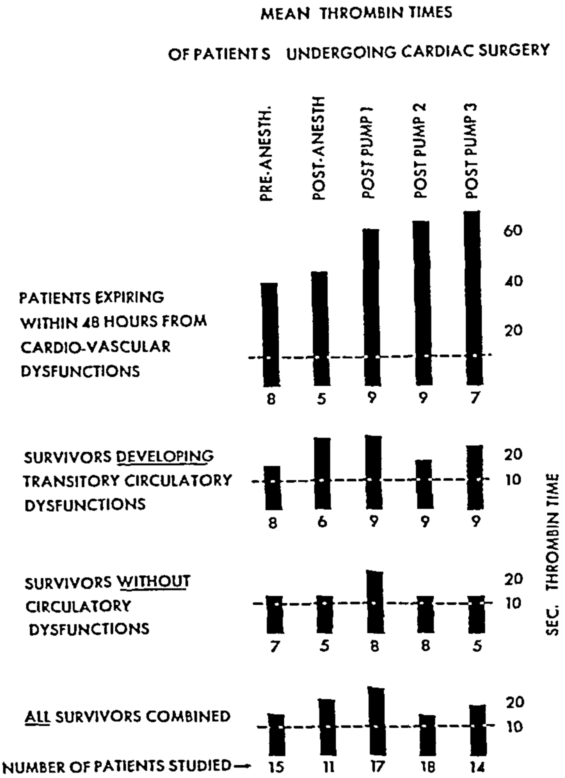

Fig. 1.—Mean thrombin times of surviving and nonsurviving patients during various phases of cardiac surgery. Dotted line represents normal values.

If the thrombin times of patients dying from cardiovascular complications within a few days are computed, the picture changes drastically. This computation has been done in the upper set of histograms of Fig. 1. The thrombin times in this group of patients were extremely long and, in several instances, no clot at all could be obtained. For the calculation of our average values, incoagulability within 5 minutes was set at 120 sec. thrombin time. The incoagulability was due to an inhibitor and not due to afibrinogenemia as demonstrated by a mixing test with normal plasma and the easy obtainability of an euglobulin clot which contains only about 25 per cent of the total plasma fibrinogen. Note the particularly gross deviations from normal during the post-pump phase. It is essential to emphasize that, in patients dying within 48 hours, the thrombin time was frequently already elevated in the control values and/or in the sample drawn after induction of anesthesia. In general, it was noted that in most of our patients exhibiting cardiovascular dysfunction during or after surgery, the elevation of the thrombin time could be demonstrated *before* the clinical symptoms became apparent (within 48 hours). Table I shows this.

TABLE I

	SURVIVORS	NONSURVIVORS
Number of patients	9	9
Patients with thrombin time above 24 sec.		
Before surgery	0	6
After surgery	2	7
Before or after surgery	2	9

Of 9 surgical patients dying from cardiovascular complications, 6 exhibited a prolongation of the thrombin time to double or more of normal values *before* the heart was opened, in contrast to 9 patients with no complication who did not show this abnormality. In 9 patients who succumbed, all had at least one very gross abnormality (above 40 sec.) of the thrombin time during the period of observation in contrast to only 2 of a group of 9 who maintained stable circulatory systems.

The group of survivors in which some cardiocirculatory disturbances developed is in an intermediate position, which becomes apparent when the percentage of the thrombin time determinations above 24 seconds is calculated for each group. The percentages are: survivors without dysfunction, 5.7 per cent; survivors with dysfunction, 25 per cent; nonsurvivors, 64 per cent.

The significance of the thrombin time is obvious when the results from the patients in whom it was possible to determine the thrombin time before *and* after induction of anesthesia, but before actual surgery, are studied (Table II). It can be seen that a prolonged thrombin time before anesthesia (control value) signifies a poor prognosis and that a rise of the thrombin time after induction of anesthesia also carries a serious prognosis.

Figs. 2 through 6 demonstrate our findings in individual examples. The arrangement of all the figures is almost identical. The fibrinolytic activity is estimated with the euglobulin technique, the only one which allows a quick measurement of fibrinolytic activity in blood uncoagulable due to the presence of clotting inhibitors.[2] The values are expressed in minutes as euglobulin lysis time, the normal values being above 120 minutes. The thrombin times are expressed in seconds, and the urokinase values in our laboratory units (specific gravity coefficient); also indicated is the surgical phase at which the samples were drawn and these data are correlated with the actual time.

Fig. 2 represents a patient who was operated upon without complications with the use of hypothermia combined with a pump-oxygenator for the suture closure of an interventricular septal defect. The euglobulin lysis time exhibits increased lysis of the control plasma, a tendency that has been frequently

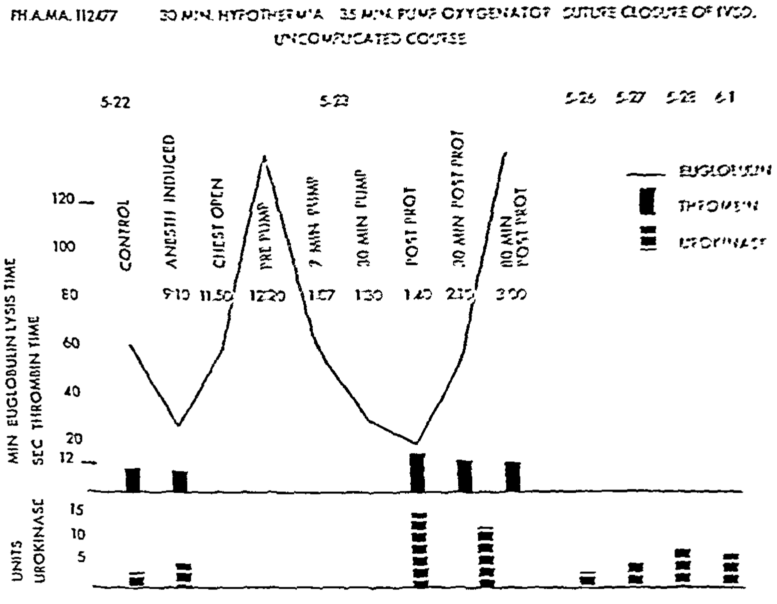

Fig. 2.—Trend of thrombin time, fibrinolytic activity, and urokinase excretion of a patient perated upon for suture closure of interventricular septal defect—30 minutes hypothermia, 35 minutes pump-oxygenator. No gross changes of thrombin time. *Note:* Increase of urokinase xcretion during the second fibrinolytic phase.

TABLE II. RESULTS FROM 15 PATIENTS IN WHOM THE THROMBIN TIME WAS DETERMINED BEFORE AND AFTER INDUCTION OF ANESTHESIA (9 PATIENTS ALIVE, 6 DEAD)

	NUMBER OF PATIENTS	ALIVE	DEAD	
Thrombin time *below* 24 sec.				
Before anesthesia	11	9	2*	18%
After anesthesia	8	7	1*	14%
Before *and* after anesthesia	8	7	1*	14%
Thrombin time *above* 24 sec.				
Before anesthesia	4	0	4	100%
After anesthesia	7	2	5	71%
Before *and* after anesthesia	4	–	4	100%

*The 2 patients in these groups who died, in contrast to the survivors, exhibited extreme prolongation of the thrombin time during the post-pump period.

If the thrombin times of patients dying from cardiovascular complications within a few days are computed, the picture changes drastically. This computation has been done in the upper set of histograms of Fig. 1. The thrombin times in this group of patients were extremely long and, in several instances, no clot at all could be obtained. For the calculation of our average values, incoagulability within 5 minutes was set at 120 sec. thrombin time. The incoagulability was due to an inhibitor and not due to afibrinogenemia as demonstrated by a mixing test with normal plasma and the easy obtainability of an euglobulin clot which contains only about 25 per cent of the total plasma fibrinogen. Note the particularly gross deviations from normal during the post-pump phase. It is essential to emphasize that, in patients dying within 48 hours, the thrombin time was frequently already elevated in the control values and/or in the sample drawn after induction of anesthesia. In general, it was noted that in most of our patients exhibiting cardiovascular dysfunction during or after surgery, the elevation of the thrombin time could be demonstrated *before* the clinical symptoms became apparent (within 48 hours). Table I shows this.

TABLE I

	SURVIVORS	NONSURVIVORS
Number of patients	9	9
Patients with thrombin time above 24 sec.		
Before surgery	0	6
After surgery	2	7
Before or after surgery	2	9

Of 9 surgical patients dying from cardiovascular complications, 6 exhibited a prolongation of the thrombin time to double or more of normal values *before* the heart was opened, in contrast to 9 patients with no complication who did not show this abnormality. In 9 patients who succumbed, all had at least one very gross abnormality (above 40 sec.) of the thrombin time during the period of observation in contrast to only 2 of a group of 9 who *maintained* stable circulatory systems.

The group of survivors in which some cardiocirculatory disturbances developed is in an intermediate position, which becomes apparent when the percentage of the thrombin time determinations above 24 seconds is calculated for each group. The percentages are: survivors without dysfunction, 5.7 per cent; survivors with dysfunction, 25 per cent; nonsurvivors, 64 per cent.

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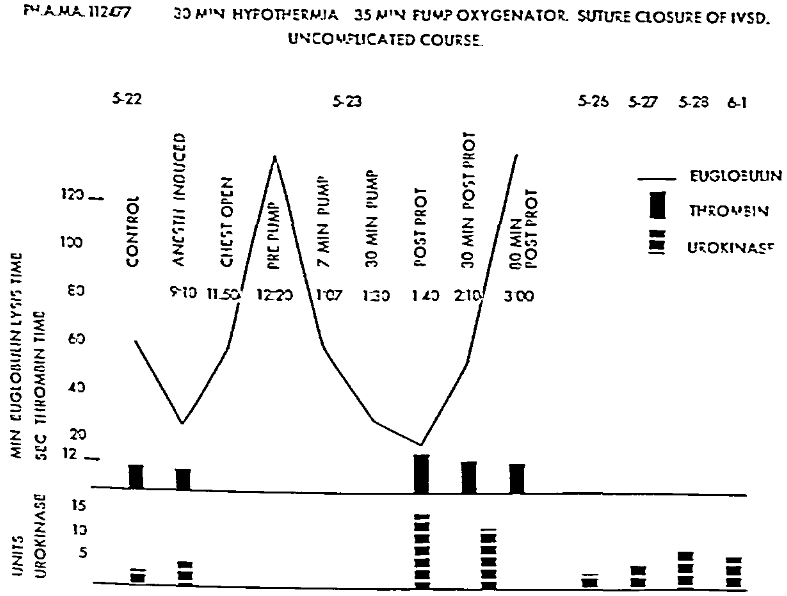

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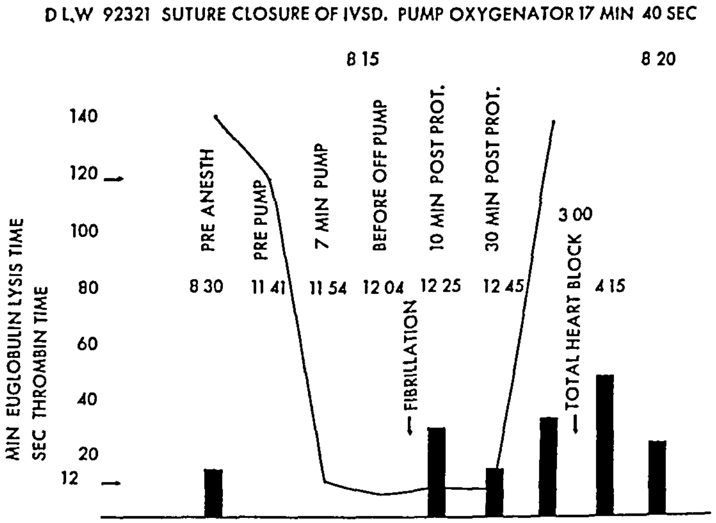
observed. This is seen in children with congenital heart disease and is enhanced by induction of anesthesia. The increase in tendency to lysis disappears as anesthesia continues, reappears during the pump phase, is enhanced by protamine injection, and finally disappears completely. The urokinase excretion also shows the usual trend: an increase concomitant with the increased lysis tendency in the late pump phase and early post-pump phase, a decrease in the first postoperative days, and then a gradual return to normal. The thrombin time itself shows no particular rise except for the first post-protamine injection sample; but here, the presence of heparin traces from the previous heparinization cannot be absolutely excluded.



PH VENOUS BLOOD	7 39	7 31	7 09	7 17
FIBRINOGEN mg %	352	165	395	229
PLATELETS IN THOUSANDS	295	38	49	37

Fig 3 —Trend of thrombin and fibrinolytic activity of a patient operated upon for suture closure of interventricular septal defect *Note* Increase of thrombin time, appearance of heart block, and strong fibrinolytic reaction combined with acidosis Pump-oxygenator: 17 minutes

Fig. 3 represents the data from a surviving patient who exhibited ventricular fibrillation during the closure of his septal defect and developed a total heart block during the immediate postoperative period. It can be seen that the thrombin times are considerably prolonged and they show a definite increase *before* the appearance of the heart block. Note also the very marked increase in fibrinolytic tendency which is sustained by acidosis, an observation which has previously been described by us.[1]

The increase in thrombin time can reach quite extraordinary proportions Figs. 4 through 6 are shown as instructive examples Fig. 4 gives the data from a patient with the tetrology of Fallot. He was operated upon with the use of the pump-oxygenator for suture closure of an interventricular septal defect and resection of an infundibular stenosis. The preoperative thrombin times were prolonged and then became indeterminable after the pump phase.

At that time, oozing was noted; however, there was no increase in fibrinolytic activity. Three grams of fibrinogen were given, the oozing subsided, and the thrombin time became measurable again. Soon it returned to immeasurable values and the oozing started again. Following this, a complete atrioventricular block developed and the thrombin time remained immeasurable during this period. In vitro, 15 mcg. of protamine sulfate per cubic centimeter added to the citrated plasma of this patient shortened the thrombin time considerably. Four hours after the last blood specimen was drawn, the patient died. It can be seen from Fig. 4 that the increase in thrombin time anteceded the cardiovascular disturbances. There was no fibrinolysis whatsoever and the incoagulability of the patient's blood was not due to afibrinogenemia but due to a very marked increase of thrombin inhibitor.

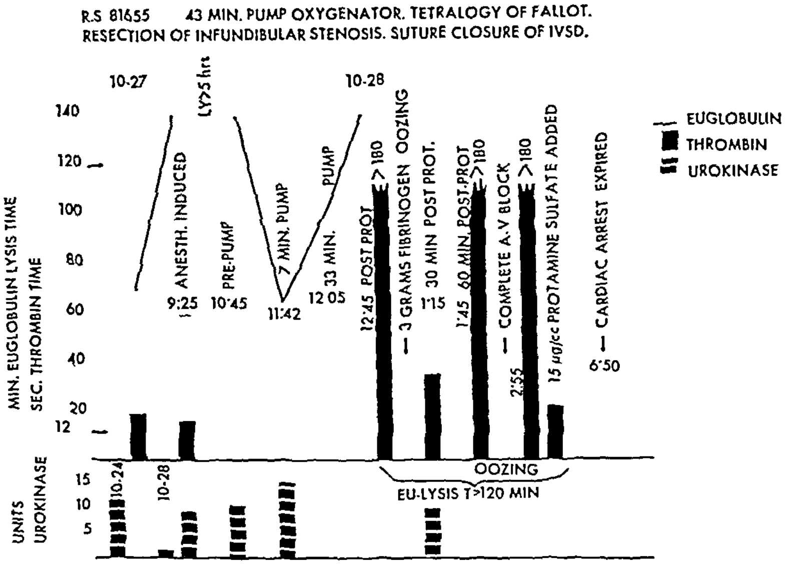

R.S 81655 43 MIN. PUMP OXYGENATOR. TETRALOGY OF FALLOT.
RESECTION OF INFUNDIBULAR STENOSIS. SUTURE CLOSURE OF IVSD.

Fig. 4.—Tetralogy of Fallot. Patient operated upon for infundibular stenosis and suture closure of interventricular septal defect. Trend of thrombin time, fibrinolytic activity, and urokinase excretion. *Note:* Gross increase of thrombin time before oozing and atrioventricular block. Pump-oxygenator: 43 minutes.

A comparable situation prevailed with the patient whose data are shown in Fig. 5. The diagnosis and the surgical procedure were similar to that in the previous patient. His thrombin times were extremely prolonged from the very beginning. The shortest value during the operative period was observed 5 minutes after injection of protamine. Thereafter, however, the thrombin time again rose to immeasurable values. About 12 hours after surgery, the patient had a cerebral vascular accident, the nature of which could not be determined. As a result of this accident, the patient had to be put in a respirator. He never regained consciousness and died 6 days later. Again in this patient, the rise of the thrombin time preceded the circulatory dysfunction. The postoperative urokinase values in this patient did not return to normal after the immediate postoperative drop, as they do in patients with normal post-surgical recovery.

Fig. 6 shows the data from a third patient with tetralogy of Fallot. In this case, hypothermia alone was used. The patient had a prolonged control thrombin time which rose to very high values after induction of anesthesia. It became immeasurable after occlusion of the circulation and remained that way. The appearance of these high values preceded a series of cardiac arrests The patient died 2 days later. There was an increase in the fibrinolytic activity during surgery but, in contrast to surviving patients, the urokinase values of this patient dropped continuously during and after surgery until his death.

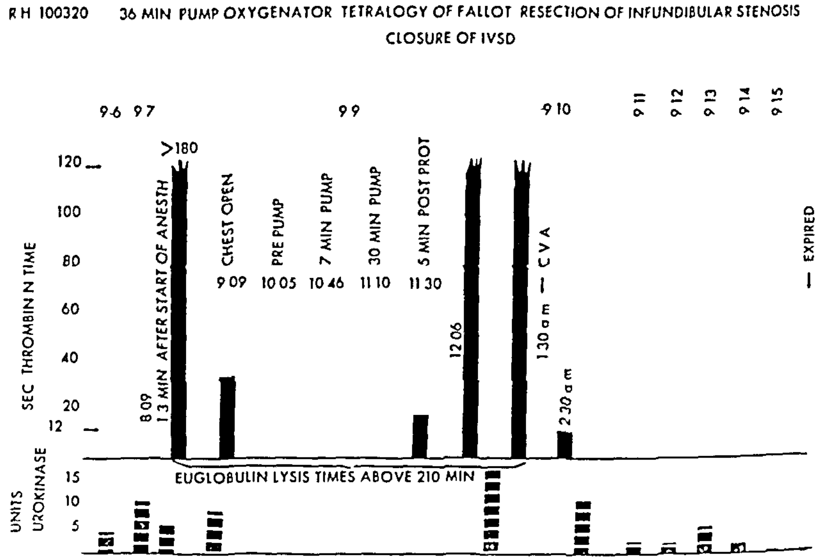


Fig. 5.—Tetralogy of Fallot Patient operated upon for resection of infundibular stenosis and closure of interventricular septal defect. Trend of thrombin time and urokinase excretion No increase in fibrinolytic activity *Note* Gross increase of thrombin time before surgery and reappearance of gross increase of thrombin time before cerebral vascular accident Pump-oxygenator: 36 minutes

The prolongation of the thrombin time which has been observed is due to a thrombin inhibitor. This is demonstrated by determining thrombin times in mixtures of the patient's plasma with normal plasma which results in a prolongation of the thrombin time of the normal plasma. Examples are shown in Table III.

Mismatched transfusions are another cause of a sudden rise of the thrombin time.[3] Here again, it was observed that the thrombin time of normal plasma

TABLE III. INCREASES IN THROMBIN TIMES OF NORMAL PLASMA BY ADDITION OF PATIENT'S PLASMA: TWO EXAMPLES

	PER CENT CONCENTRATION OF PLASMA		THROMBIN TIME (SEC.)
	PATIENT	NORMAL	
Case 1	100	—	180
	—	100	11
	25	75	17
	75	25	37
Case 2	100	—	240 +
	—	100	7
	40	60	240 +
	20	80	20

was prolonged by the addition to it of the plasma of the patient. The release of a "heparinoid" anticoagulant was studied extensively with the thrombin time in dogs exposed to mismatched transfusions by McKay and his colleagues.[4]

A marked prolongation of the thrombin time was also seen by us, combined with an increase in fibrinolytic activity and oozing tendency, in a patient being prepared for portocaval shunt, and in patients with severe pulmonary lung embolism.

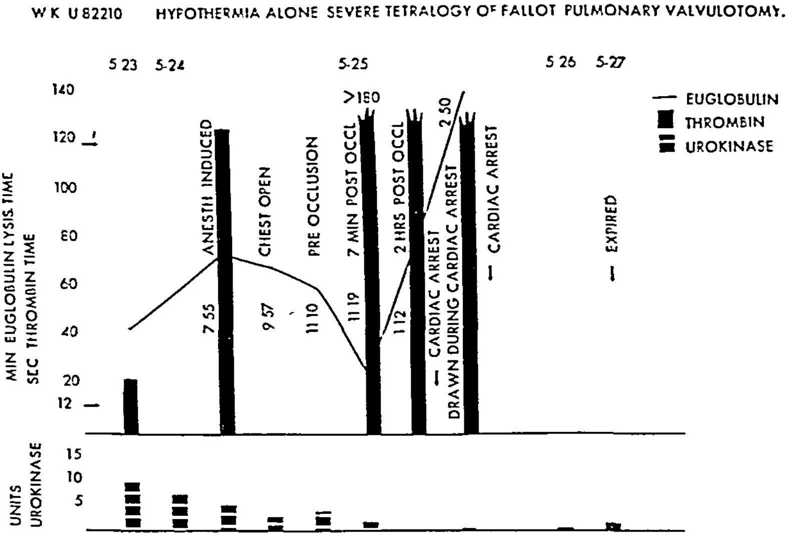


Fig. 6.—Tetralogy of Fallot. Patient operated upon for pulmonary valvulotomy under hypothermia. *Note:* Increase thrombin time in control sample and gross increase during anesthesia and surgery preceding a series of cardiac arrests. Steady drop of urokinase excretion until death.

DISCUSSION

The immediate problem raised by these observations is the nature of the anticoagulant causing the clotting defect. It is not yet possible to say whether this substance is heparin, or not. It is sometimes neutralized by protamine both in vitro and clinically but, on other occasions, protamine is quite ineffectual and excessive quantities are required for neutralization of the thrombin inhibitor in vitro. Possibly two related compounds are involved; for instance, heparin and Loeliger's[5] antithrombin V, which immediately neutralizes thrombin but is not neutralized by protamine.

It is well known that a variety of stimuli, including experimental shock, may trigger the release of heparin and related substances into the general circulation; but observations of the release of an anticoagulant during surgery in man are scant. Perlick[6] noted a marked increase in "heparin-antithrombin" levels during prostatectomy on hypotensive patients, but did not see this change in those operated upon without hypotension, although there was a release of "heparin-antithrombin" in patients with vasolability. Weiss[15] mentions 2 patients who presented a "heparin-like" syndrome after open-heart surgery with hypothermia and Muller[14] reported on a patient who exhibited a prolonged thrombin time which was not corrected by administration of protamine after disconnection of the pump-oxygenator. The plasma of this patient prolonged the thrombin time of normal plasma. We reported an increase of thrombin inhibitor in cardiac patients operated upon under hypothermia.[9] However, these increases were moderate compared with the ones previously reported and with those described in the present study of patients of a different type and operated upon with a different technique.

Experimentally, Lasch[7] demonstrated a marked release of heparin during the rewarming phase in hypothermic dogs undergoing heart surgery. Kolff and co-workers[8] observed in dogs a reappearance of delayed clotting several hours after protaminization and designated this phenomenon a "heparin-rebound" effect; but, these observations might well be related to the findings described here.

It has been reported that during the course of a variety of diseases, such as disseminated lupus erythematosus, metastatic carcinoma of the liver, cirrhosis of the liver, malabsorption syndrome, multiple myeloma, pre-eclampsia, and eclampsia, an anticoagulant may appear which produces a prolongation of the thrombin time accompanied by a hemorrhagic diathesis uncorrectable by the administration of protamine sulfate. (For literature, see Favre-Gilly and collaborators.[10]) In these diseases, the clotting defect appears gradually but, during surgery, it appears suddenly, suggesting the possibility of an abrupt release of the anticoagulant from storage organs. The same situation obtains in experimental anaphylactic shock during which an anticoagulant of antithrombin type is momentarily released which results in incoagulability and is accompanied by a reduction of the surface tension of the blood. If the shock is lethal, the anticoagulant can be demonstrated until the death of the animal. Near lethal Adrenalin injections produce the release of an antithrombin substance in contrast to small doses which enhance coagulation.[11] Pharmacologically, active compounds acting on the autonomic nervous system, as well as pain, mechanical stimulation of vagosympathetic or parasympathetic nerves, or of certain parts of the cortex, bring about a very swift change of the activity of a variety of clotting components.[12, 13] Increased sympathetic tone is likely to enhance the coagulation in contrast to vagus stimulation which exerts an inhibiting effect. Vagal tone tends to increase the heparin antithrombin. There are some contraindications in the literature which might be explained by the observation[13] that the changes in the activity of the coagulation factors are dependent upon the tonus of the autonomic system at the moment of stimulation.

Therefore, the release of thrombin inhibiting substances may depend upon the status of the autonomic nervous system of the patient. Certain changes in its reactivity may induce the release of inhibitors and simultaneously influence the cardiovascular system in such a way that it responds abnormally to surgical and other stresses. If this assumption is correct, our observation that increase in thrombin time heralds the cardiovascular disturbances might be explained on this basis. Interestingly enough, the highest preoperative thrombin times were observed in patients with tetralogy of Fallot. De Sario[14] also found increased antithrombin activity in the patients with tetralogy of Fallot. There is frequently a high risk in operating on these patients.

Bleeding, itself, was a problem in only 2 of our patients and, therefore, is not an inevitable consequence of an elevation of the thrombin time. This phenomenon is more likely to occur when the inhibitor increase coincides with very marked fibrinolytic activity. Severe bleeding of this type was seen in 1 patient, reported in detail earlier.[1] A second patient (Fig. 4) exhibited a considerable oozing tendency concomitant with a very marked increase in thrombin time.

Bleeding may be treated by the use of fibrinogen and ACTH infusions, $CaCl_2$ and Adrenosem. Protamine may be tried but it occasionally enhances or initiates a fibrinolytic reaction. The maintenance of an adequate blood pressure by the adequate replacement of blood loss and other means is of crucial importance.

It would seem likely that, during the past, incoagulability of blood developing during surgery or under other circumstances may well have been misdiagnosed as afibrinogenemia, when, in reality, a strong thrombin inhibitor was present.

SUMMARY

Serial thrombin time determinations were done in 27 patients undergoing cardiac surgery. Twenty-six were operated upon with the pump-oxygenator, with or without hypothermia, and 1 with hypothermia alone. In the patients who died after the procedure, a marked elevation of the thrombin time was found in the control specimen, and a marked rise after induction of anesthesia, but before the surgery. A sudden rise of the thrombin time during the post-pump phase heralds cardiovascular dysfunction which may or may not lead to death. Postoperative death was associated with the greatest elevations of the antecedent thrombin times. The mechanism underlying these findings is discussed.

We wish to thank Mrs. Edith von Kaulla for her technical assistance in this study.

REFERENCES

1. Von Kaulla, K. N., and Swan, H.: Clotting Deviations in Man During Cardiac Bypass: Fibrinolysis and Circulating Anticoagulants, J. THORACIC SURG. 36: 519, 1958.
1a. Muller, W. H., Jr.: Discussion of von Kaulla and Swan.[1]
2. Von Kaulla, K. N., and Schulz, R. L.: Methods for the Evaluation of Human Fibrinolysis. Studies With Two Combined Techniques, Am. J. Clin. Path. 29: 104, 1958.
3. Favre-Gilly, J., Thouverez, J. P., and Revol, L.: Sur trois cas de diathese hemorrhagique par anticoagulant spontané, Tr. 6th Cong. European Soc. Haematology, Copenhagen, 1957, S. Karger, p. 524.
4. McKay, D. G., Hardaway, R. M., Wahli, H. G., Edelstein, R., and Tartock, D. E.: Alterations in Blood Coagulation Mechanism After Incompatible Blood Transfusion, Am. J. Surg. 89: 583, 1955.
5. Loeliger, A., and Hers, J. F. Ph.: Antithrombinaemia With Hemorrhagic Diathesis in a Case of Rheumatoid Arthritis With Hypergamma Globulinaemia. Antithrombin V, Thromb. Haem. 1: 499, 1957.

6. Wendt, H., Perlick, E., and Seyffarth, G. H.: Zur Blutung und Nachblutung bei der Prostatektomie, Langenbecks Arch. klin. Chir. 286: 322, 1957.
7. Lasch, H. C., Sessner, H. H., Spohn, K., Kobb, E., Heinzel, J., and Kratzers, R. Blutgerinnung bei tiefer Hypothermia, langdauerndem Herz Kreislaufstillstand und die Wiederbelebung, Klin. Wchnschr. 37: 182, 1959.
8. Kolff, W. S., Effler, D. B., Groves, L. K., Peereboom, G., and Moraca, P. P. Disposable Membrane Oxygenator (Heart-Lung Machine) and Its Use in Experimental Surgery, Cleveland Clin. Quart. 23: 69, 1956.
9. Von Kaulla, K. N., and Swan, H.: Studies of the Clotting Mechanism in Man During Open-Heart Surgery Associated With Hypothermia, J. THORACIC SURG. 36: 857, 1958
10. Favre Gilly, J., Simon, B., *Thouverez, J. P., and Diebold, Ch.: Diathese hemorrhagique* femine avec presence dans le sang d'une antithrombine du type de l'heparine, Sang 29: 398, 1958.
11. Zunz, E., and La Barre, J.: Contribution a l'etude des modifications de la coagulation du sang au cours du choc anaphylactique chez le chien, Arch. internat. de physiol. 25 221, 1925
12. Natcheff, N., Nicolaff, A., Pirvova, B., and Tancoff, N.: Sur la regulation nerveuse de la coagulation du sang, J. physiol. Paris 49: 1091, 1957.
13 Schimpf, Kl., Petry, H. J., and Lasch, H. G.: Die Wirkung von Sympatholytika und Parasympathicolytica auf das Gerinnungssystem des Menschen, Deutsches Arch. klin. Med. 205: 166, 1958
14. De Sario, P. H.: L'attività antitrombinica nei cardiopatici congeniti, Minerva cardio angiol. 5: 102 105, 1957.
15. Weiss, A. W., Gilman, I. S., Catenacci, A. Z., and Osterberg, A. E.: Heparin Neutralization *With Polybrene Administered Intravenously*, J. A. M. A. 166: 603, 1958

TRAUMATIC ANEURYSM OF THE THORACIC AORTA SIMULATING COARCTATION

A Case Report

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TRAUMATIC thoracic aneurysms have been described as a pathologic entity for many years[1-4] but only occasionally present as a surgically correctable lesion. This lesion has been encountered only twice among 126 patients with thoracic aneurysm operated upon at Presbyterian Hospital. During recent years, excisional therapy has proved increasingly safe and effective, emphasizing the need for increasing our knowledge of the clinical course of this entity.

The majority of patients receiving trauma sufficient to rupture the aorta die almost immediately. Attesting to this is the fact that the largest reported series of 72 traumatic aneurysms was among 7,000 consecutive autopies reported from the Chief Medical Examiner's office of New York City.[5] The fate of those patients who survive the initial aortic injury appears variable and for the most part unpredictable. Survival and the subsequent clinical course must depend upon the depth and size of the aortic tears and the ability of the residual media, adventitia, and adjacent structures to buttress the laceration and hematoma against constant aortic pressure.

The development of a widened mediastinum and clouding of the aortic knob, following severe chest trauma, should strongly suggest that rupture of the aortic wall may have occurred. The subsequent x-ray appearance of a bulging or double contour in the area of the aortic arch, during the first to fourth weeks following injury, is diagnostic of traumatic aneurysm, or, better termed, a false aneurysm. The subsequent course of these lesions has been difficult to evaluate but, based on a summary of available reports of patients surviving the first 10 hours after injury, approximately 40 per cent of these aneurysms rupture within the first 60 days (Table I). Steinberg[15] has recently emphasized that a certain number of these lesions become chronic, stable, and ultimately show calcification by roentgenogram. Unfortunately there is no satisfactory way to anticipate which of the acute lesions will become chronic and stable from

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those that will rupture. In the case to be presented, there developed a clinical picture associated with a traumatic aneurysm of the descending thoracic aorta that has not previously been described; an awareness of this sequence of events may aid in the diagnosis and mangement of future cases.

TABLE I. COURSE OF PATIENTS SURVIVING 10 HOURS AFTER INJURY

	NUMBER OF CASES	CHRONIC	PROGRESSIVE	SURGICAL CURE	DEATH AFTER SURGERY	RUPTURE
Bradford and Johnston[6]	1					5 wk.
Bahnson[7]	1			1		
Corbitt[8]	1					20 hr.
Eiseman and Rainer[9]	6	2	1	1	1	9 da.
Forbes[10]	1					30 hr.
Goyette et al.[11]	3	2			1	
Hardin et al.[12]	1				1	
Henning and Agmar[13]	1					48 hr.
Hollingsworth et al.[14]	4	2	1	1		
Kuhn[15]	1					10 da.
Rice and Wittstruck[16]	1					5 wk.
Sarot and Lazzaieni[17]	1			1		
Steinberg[18]	5	4			1	
Storey et al.[19]	2			1		12 da.
Stranahan et al.[20]	1			1		
Strassman[5]	4					(4) 12 and 18 hr.
Ware et al.[21]	1				1	
Wyman[22]	3					(3) 11 hr.; 15 hr.; 8 da.
Zehnder[23]	1					4½ da.
Totals	39	10	2	6	5	16

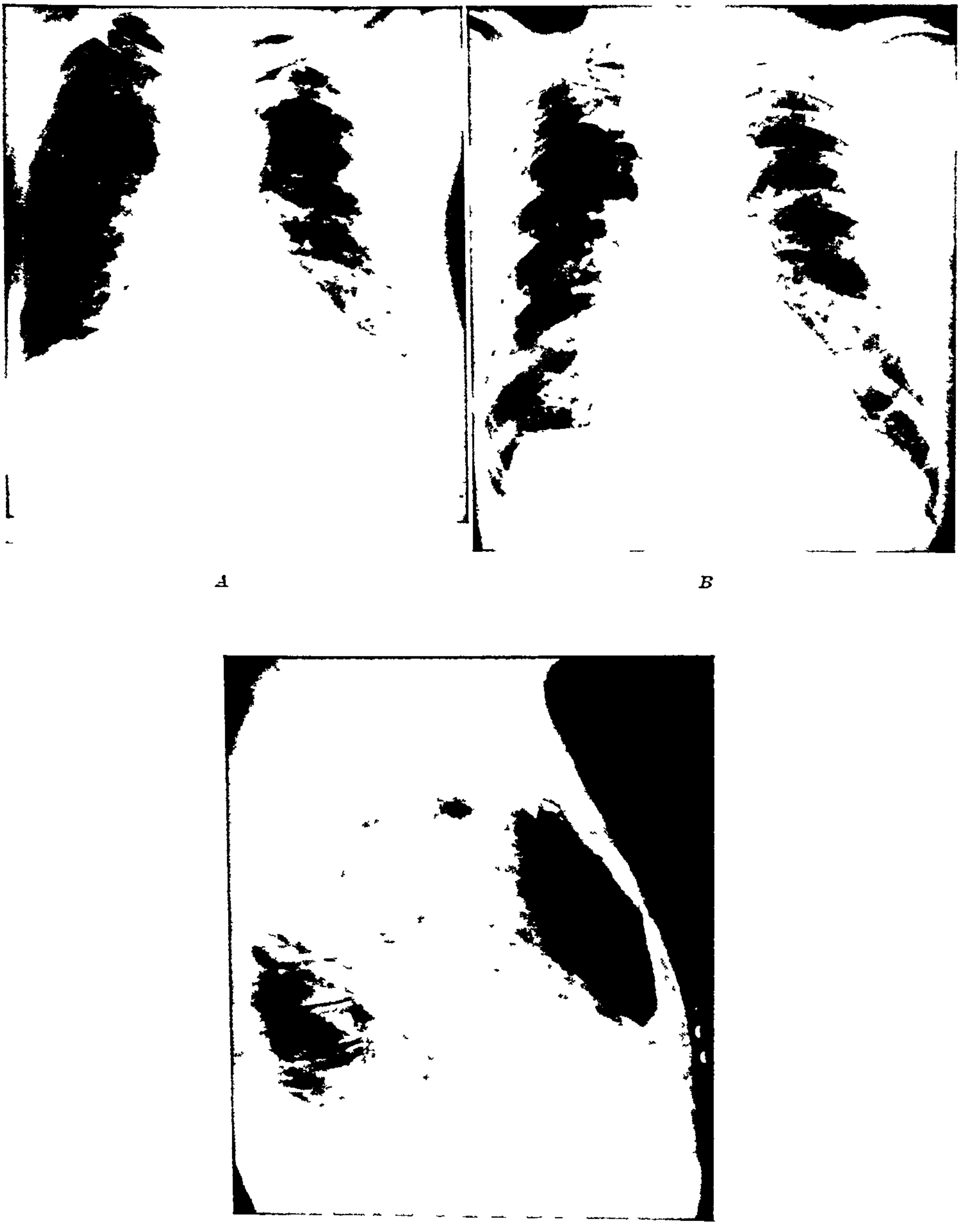
CASE REPORT

W. R., a 48-year-old man, was struck by a truck on Feb. 28, 1958. On admission to the hospital he was in extreme respiratory distress. A roentgenogram of the chest confirmed the clinical impression of multiple rib fractures and a bilateral hemothorax. Thoracentesis and supportive therapy relieved respiratory distress and blood pressure was maintained at 150/80 mm. Hg.

Ten days following injury the patient developed an episode of severe right chest and substernal pain accompanied by dyspnea, hyperpnea, and sweating. At this time the blood pressure was recorded as 220/100 mm. Hg. The electrocardiogram remained essentially unchanged throughout this period. Episodic pain recurred almost daily and alternating auricular fibrillation and flutter with a 2:1 block developed on the twentieth hospital day.

The patient was discharged on the thirty-first hospital day. Although digitalized he was readmitted 8 days later in acute left ventricular failure. The patient responded promptly to oxygen, diuretic drugs, and an increased dosage of digitalis. Arterial tension in both arms was recorded as 240/80 mm. Hg. A chest roentgenogram made 41 days after the injury now showed a double contour enlargement in the region of the aortic arch which suggested aneurysmal formation (Fig. 1). Chest pain and cardiac failure recurred and the patient was transferred to Presbyterian Hospital on April 28, 1958.

On admission the patient was dyspneic, orthopneic, and cyanotic, with a rapid irregular pulse. Arterial pressure in the right arm was 220/80, in the left arm 240/80 mm. Hg. Carotid pulses were equal to palpation. The blood pressure was recorded as 90/0 mm. Hg in both lower extremities and pulsations in the abdominal aorta could not be felt. The heart was enlarged to the anterior axillary line and a soft systolic murmur could be heard over



A

B

C.

Fig 1 —A, Roentgenogram of the chest taken 2 weeks following injury shows evidence of multiple rib fractures and some widening of the mediastinum.

B, Subsequent x-ray studies 2 months following injury clearly demonstrated the prominent aorta arch with a double contour.

C, The lateral view shows the aneurysm arising in the proximal descending aorta.

the left chest anteriorly and posteriorly. The patient was placed on a strict cardiac regimen and signs and symptoms of cardiac failure resolved within 48 hours after admission. On May 14, an angiocardiogram was performed in two projections which confirmed the conventional roentgenographic appearance of an aneurysmal dilatation of the aorta just beyond the origin of the left subclavian artery.

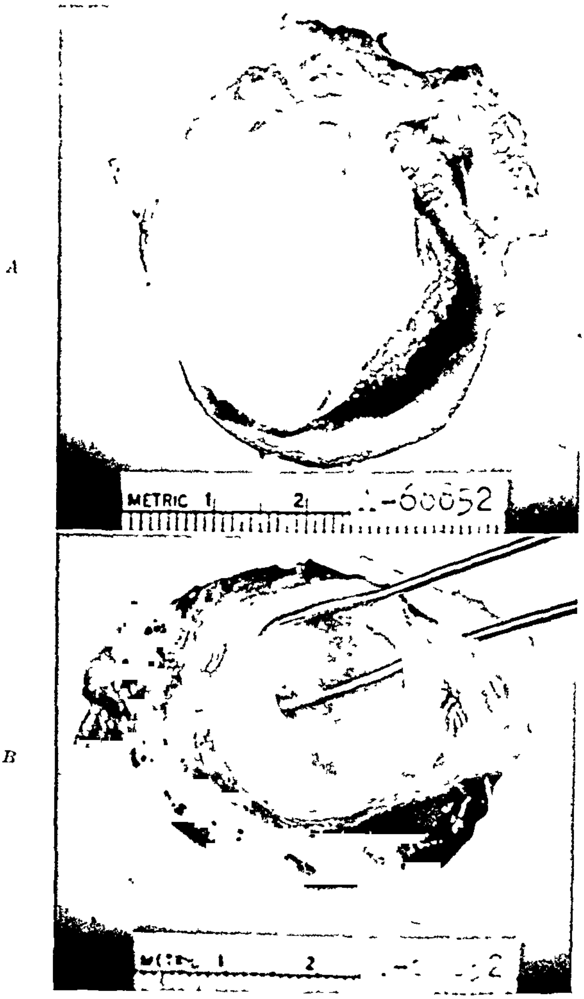


Fig. 2.—*A*, The specimen shows the hematoma sac as viewed from the proximal end of the aortic segment.

B, An intact aortic wall is seen distally. Microscopically the hematoma separated the adventitia from the media with infarction noted in the outer two thirds of the media.

On May 20, approximately 3 months following injury, exploratory left thoracotomy was performed. An aneurysmal dilatation of the thoracic aorta was noted just distal to the left subclavian artery, measuring approximately 6 by 8 by 8 cm. Excision of the aneurysm was possible during partial perfusion of the distal aorta by a left atrium to left femoral artery bypass with a Sigmamotor pump.[24] A perfusion rate of 2,200 c.c. per minute was required to control proximal aortic hypertension. A preclotted crimped Dacron prosthesis* was inserted. On the day following surgery, the patient's blood pressure was 130/80 mm. Hg in all extremities. The postoperative course was uneventful except for an episode of auricular fibrillation occurring on the second postoperative day which responded to increasing doses of digitalis. Since discharge the patient has remained normotensive and is well 1 year following surgery.

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*Ethigraft available from Ethicon Inc., Somerville, N. J.

The pathologic specimen (Fig. 2) showed the large hematoma space outside the aortic lumen. The hematoma presented outside the media of the aortic wall microscopically, which probably explains why the dissection did not progress along the aorta as occurred in the case reported by Rice[16] of a pregnant woman at term, following chest injury. The diagram in Fig. 3 shows the probable sequence of events following aortic tear with formation of the partially obstructing hematoma.

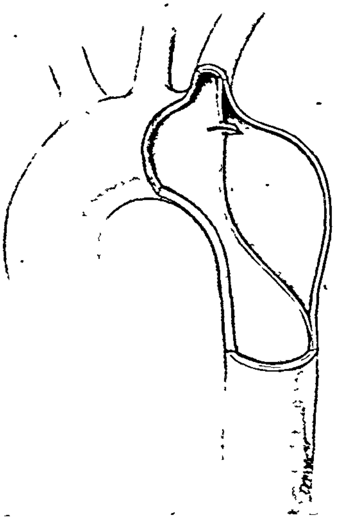

Fig. 3.—The schematic diagram illustrates the location and obstructing nature of the hematoma mass following the aortic wall dissection through the intimal tear.

DISCUSSION

The recent publications of Steinberg[18] and others[9] have raised a question as to the advisability of operating on a patient simply because the roentgenographic diagnosis of post-traumatic aneurysm is made. If observation proves to be an accepted form of clinical management, then a recognition of changing hemodynamics in the peripheral vascular system may be significant evidence of active bleeding and impending disaster following chest injury, as is well recognized in dissecting aneurysms. It is quite possible that the sudden development of hypertension proximal to an aortic hematoma may be a cause of sudden rupture late in the course of the aneurysm. Such a sequence of events is suggested in Case 3 reported by Eiseman,[9] although blood pressures were not reported. The patient developed a left hemothorax on the ninth post-injury day. Two hours following this he complained of numbness in his feet and femoral pulses disappeared. The patient suddenly then went into shock and subsequently died immediately after resection of a ruptured aneurysm of the thoracic aorta.

It is apparent that when rupture occurs, attempts at surgical correction have been associated with a high mortality. With the present-day use of atrial-femoral bypass, resection of aneurysms of the descending aorta can be carried out with a mortality of approximately 19 per cent,[25] as compared to 27 to 50 per cent using hypothermia or external shunts. There seems then little reason for delaying early surgical excision of an acute traumatic aneurysm or of a chronic symptomatic lesion, once the diagnosis has been established. Observation may be justified in the chronic, stable, calcified aneurysms if careful follow-up is available. Careful repeated records of peripheral pulses, particularly the femoral pulses, in patients following chest injury may give valuable information in the diagnosis and management of a traumatic aneurysm, and indeed may be an early sign heralding disaster.

SUMMARY

1. A case of post-traumatic thoracic aortic aneurysm has been described which presented a hemodynamic picture simulating coarctation of the aorta.

2. A careful apprasial of peripheral pulses in patients following chest injury may give valuable information in establishing a course of management.

REFERENCES

1. Rindfleisch, E.: Zur Entstehung und Heilung des Aneurysma dissecans aortae, Virchows Arch. f. path. Anat. 131: 374-378, 1893.
2. Kemp, P. R.: Traumatic Rupture of the Aorta, Lancet 1: 953, 1923.
3. Kleinsasser, L. G.: Traumatic Rupture of the Thoracic Aorta, Ann. Surg. 118: 1071, 1943.
4. Jay, J. B., and French, S. W., III: Traumatic Rupture of the Thoracic Aorta: Review of Literature and Case Report, A. M. A. Arch. Surg. 68: 657-662, 1954.
5. Strassman, G.: Traumatic Rupture of Aorta, Am. Heart J. 33: 508-515, 1947.
6. Bradford, B., Jr., and Johnston, F. L.: Traumatic Rupture of the Aorta, Surgery 28: 893, 1950.
7. Bahnson, H. T.: Definitive Treatment of Saccular Aneurysms of the Aorta With Excision of the Sac and Aortic Suture, Surg. Gynec. & Obst. 96: 383, 1953.
8. Corbitt, A. W., and Mathews, A. R. K.: Rupture of the Aorta; A Case Report With Discussion, West Virginia M. J. 33: 372, 1937.
9. Eiseman B., and Rainer, W. G.: Clinical Management of Posttraumatic Rupture of the Thoracic Aorta, J. Thoracic Surg. 35: 347-358, 1958.
10. Forbes, G.: Traumatic Rupture of the Aorta, Brit. M. J. 2: 400, 1944.
11. Goyette, E. M., Blake, H. A., Forsee, J. H., and Swan, H.: Traumatic Aortic Aneurysm, Circulation 10: 824-828, 1954.
12. Hardin, C. A., Reisman, K. R., and Dimond, E. G.: The Use of Hypothermia in the Resection and Homologous Replacement of the Thoracic Aorta, Ann. Surg. 140: 720, 1954.
13. Henning, B. H., and Agmar, A. R.: Traumatic Rupture of the Thoracic Aorta; Report of a Case, Mil. Surgeon 103: 260, 1948.
14. Hollingsworth, R. K., Johnston, W. W., and McCooey, J. F.: Traumatic Saccular Aneurysm of the Thoracic Aorta, J. Thoracic Surg. 24: 325, 1952.
15. Kuhn, L. P.: Traumatic Rupture of the Thoracic Aorta With Review of 55 Abdominal Injuries, Illinois M. J. 47: 420, 1925.
16. Rice, W. G., and Wittstruck, K. P.: Acute Hypertension and Delayed Traumatic Rupture of the Aorta, J. A. M. A. 147: 915, 1951.
17. Sarot, I. A., and Lazzarini, A. A.: Resection of Aneurysms of the Aortic Arch and Descending Aorta: Permanent "By-Pass" Homograft, Tr. Am. Coll. Cardiol. 5: 175A, 1955.
18. Steinberg, I.: Chronic Traumatic Aneurysm of the Thoracic Aorta, New England J. Med. 257: 913-918, 1957.

19. Storey, C. F., Nardi, G. L., and Sewell, W. H.: Traumatic Aneurysm of Thoracic Aorta: Report of Two Cases, One Successfully Treated by Resection and Graft-Replacement With Aid of Shunt, Ann. Surg. 144: 69-78, 1956.
20. Stranahan, A., Alley, R. D., Sewell, W. H., and Kausel, H. W.: Aortic Arch Resection and Grafting for Aneurysm Employing an External Shunt, J. THORACIC SURG. 29: 54, 1955.
21. Ware, P. F., Adler, R. H., and Hyter, C. S.: Traumatic Aneurysm of the Thoracic Aorta, U. S. Armed Forces M. J. 6: 1674-1690, 1955.
22. Wyman, A. C.: Roentgenologic Diagnosis of Traumatic Rupture of Thoracic Aorta, A. M. A. Arch. Surg. 66: 656-663, 1953.
23. Zehnder, M. A.: Delayed Posttraumatic Rupture of the Aorta in a Young Healthy Individual After Closed Injury, Angiology 7: 252, 1956.
24. Cooley, D. A., De Bakey, M. E., and Morris, G. C.: Controlled Extracorporeal Circulation in Surgical Treatment of Aortic Aneurysm, Ann. Surg. 146: 473-485, 1957.
25. De Bakey, M. E., Cooley, D. A., Crawford, F., and Morris, G. C.: Aneurysms of the Thoracic Aorta, J. THORACIC SURG. 36: 393-420, 1958.

AN IMPROVED CAVAL CATHETER FOR CARDIAC BYPASS

R. O. Heimbecker, M.D., Toronto, Ontario*

Caval catheters must be very accurately placed in order to achieve free venous return. During the course of a long perfusion they will often shift out of position, especially if there is considerable manipulation. Moreover, the usual fixation of the catheter to the atrial appendage does not give adequate immobilization of the catheter tip.

Bardic venous catheters are firmly tied with a loop of umbilical tape, before autoclaving (see figure). After cooling, a permanent circumferential groove will be present, which will not significantly encroach on the catheter lumen. This groove is then engaged by the caval tape when total bypass begins. Perhaps it is preferable to pass the caval tape around the vena cava *twice*, to give complete fixation of the catheter tip. The catheter tip is then firmly anchored in accurate position, regardless of subsequent manipulation of the heart and catheters.

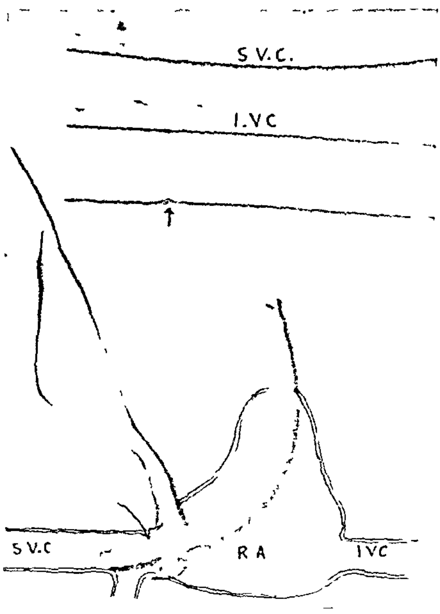

Fig. 1.

This modification has been especially useful in the superior caval type of atrial defect, in which accurate position of the catheter tip is so essential. It is also useful in septum primum defects, in which considerable traction may be applied to the catheters.

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*Research Associate of the Ontario Heart Foundation.

Announcements

THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

Notice of Annual Meeting

The Forty-first Annual Meeting of The American Association for Thoracic Surgery will be held April 24, 25, and 26, 1961, in Philadelphia, Pennsylvania. Headquarters will be the Sheraton Hotel.

Requests for Hotel Reservations

These should be mailed directly to Mr. Brian Kirby, Reservation Manager, Sheraton Hotel, Philadelphia 3, Pennsylvania. Please mention this Association, the type of accommodation desired, the date, and approximate hour of arrival and departure. If accommodations are desired elsewhere please communicate directly with the hotel of your choice.

Material for the Program

SCIENTIFIC PAPERS.—Abstracts of all papers proposed for presentation at the 1961 meeting *must be received on or before* **November 15, 1960,** otherwise they will not be considered by the Program Committee. These should be labeled "For Thoracic Surgery Forum" or "For Regular Program" depending upon the nature of the subject matter, in the same manner as in previous years. They should contain from 200 to 250 words that accurately reflect the content of the completed paper.

Six, repeat, six clearly legible copies of *each* abstract must be sent to Miss Ada Hanvey, Administrative Assistant, The American Association for Thoracic Surgery, 308 Carondelet Building, 7730 Carondelet Avenue, St. Louis (Clayton) 5, Missouri.

Essayists selected for the program are reminded that papers presented at the meeting *must* be handed to the secretary *immediately* after their presentation. If they are not ready at that time there is a chance that they will not be published in THE JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY.

Applications for Membership

Applications for Associate Membership in the Association must be received by the Membership Committee *not later than* **November 15, 1960,** otherwise the application will be deferred for consideration until the 1962 meeting.

Applicants must be sponsored by three Active or Senior Members of the Association. In addition to the signature on the application form, the sponsors will forward a *separate* letter concerning the applicant directly to:

Frank Gerbode, M.D.
Chairman of the Membership Committee
Presbyterian Medical Center
San Francisco 15, California

Sponsors are reminded that *new* letters of recommendation must be forwarded to the Chairman of the Membership Committee should their applicants be held over for reconsideration a *second year.*

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In Memoriam

EDWARD JAMES O'BRIEN

DR. EDWARD JAMES O'BRIEN died at 10 A.M., Oct. 19, 1959, at Harper Hospital, Detroit, Michigan. He died as the result of two separate carcinomas, one of the prostate and one of the lung. He was born at Hatley, Wisconsin, and was, at the time of his death, 72 years of age. He grew up in Wisconsin until high school age, when he moved to Alpena, Michigan, where he lived with his sister, Mrs. Elizabeth Bonneville and her husband, Dr. Louis Bonneville, a practitioner there for many years.

When his high school education was finished he entered the Detroit College of Medicine, now the Medical College of Wayne State University, and was graduated in 1909. He entered the intern service at Harper Hospital, Detroit, Michigan, where he served two years. He entered the practice of medicine in 1911 in Detroit.

At the outbreak of World War I in 1917 he joined the Harper Hospital Unit, known as Base Hospital 17, and served until sent home because of a duodenal ulcer. This disorder continued to plague him during the rest of his life.

He was appointed to the staff of Harper Hospital and the Herman Kiefer Hospital, the latter being the infectious disease hospital of Detroit. At that time, tuberculosis was becoming a problem in a growing industrial city, and its control was essential. Dr. Burns Amberson was appointed Controller. It has often been said that because of tuberculosis in his immediate family Dr. O'Brien became interested in the problem of tuberculosis. This is not the case; it was Burns Amberson who influenced him to enter the field of thoracic surgery.

Thus, in 1926 he embarked on a study program. There were not many places to go, for the art was new. On his return, he, for a period, operated in an old wooden building on the grounds at Herman Kiefer Hospital. It had previously been a boiler room.

In 1928 he became Chief of Thoracic Surgery at Herman Kiefer Hospital and then limited his practice to thoracic surgery. In 1930 he became Chief of Thoracic Surgery at Harper Hospital. These positions he held for many years.

The State of Michigan formed a State Sanitarium Commission, and he was appointed a member of this Commission in 1928. He remained as a member and, most of the time, as its Chairman until 1950, when Governor Williams removed him because of disagreements

He served for many years as a Clinical Professor of Surgery at Wayne State University and previous to that as a preceptor in anatomy at the Detroit College of Medicine.

Photo from The Detroit News

EDWARD JAMES O'BRIEN

The historical side is ended This now is an analysis of the man. The writer was associated with him for over twenty-five years. His main interest was always in the field of tuberculosis He was Irish and a good politician, and he used it to the advancement of care for the tuberculous sick Almost single-handed he built institutions for the care of this disease, not only in Detroit but in the entire State. He labored tirelessly until at an early date Michigan had the most adequate hospital treatment, and control system in this field.

He was long a member of this Association, served on its Council and became its President His affection for this Association was great.

He was a man of strong opinions. He could be kind. He could be most unkind. His was a restless soul. He did the right as he saw it. He was a stormy petrel in a wind-swept sea, but when the evening came there was peace at last.

WM. M. TUTTLE, M D.

Original Communications

THE USE OF DIRECT STIMULATING MYOCARDIAL ELECTRODES IN COMPLETE ATRIOVENTRICULAR BLOCK

Bernard S. Levowitz, M.D. (by invitation), William B. Ford, M.D., and James W. Smith, Jr., M.D. (by invitation), Pittsburgh, Pa.

ACQUIRED complete atrioventricular dissociation with critically low ventricular rates has been successfully treated by external stimulation of the myocardium through the chest wall by skin electrodes.[1, 2] Prolonged application of this method, until a sustaining rhythm is restored, is poorly tolerated since it is often associated with pain, violent muscular contractions, skin burns, and superficial ulcerations. Stimulation of the heart through a direct myocardial electrode has been utilized for extended periods in the management of complete heart block following open-heart surgery, but has not been accompanied by these undesirable sequelae.[3] This technique has therefore been suggested for cases of acquired complete heart block which have proved refractory to medical management. Our experiences with 3 patients in whom myocardial electrodes and an artificial pacemaker were employed for the treatment of persistent Stokes-Adams seizures are described in this presentation.

CASE REPORTS

CASE 1.—H. S. was a 77-year-old white man who was admitted to the Presbyterian Hospital on July 29, 1959, supported by an external pacemaker.

The patient's past history disclosed that he had been hospitalized for a myocardial infarct in November, 1957, from which he had recovered satisfactorily. On June 6, 1959, he was again hospitalized at the Fairmont General Hospital, Fairmont, West Virginia, with a diagnosis of acute myocardial infarction and a complete heart block caused by arteriosclerotic cardiovascular disease. Electrocardiograms showed a complete atrioventricular dissociation with an idioventricular rate of 30 per minute (Fig. 1). The patient appeared to respond to oxygen and hydroxyamphetamine hydrobromide. However, on the following day, he complained of oppressive substernal pain, had a short episode of syncope and became cyanotic and hypotensive. His pulse rate fell to 20 per minute. Despite the administration of epinephrine and isoproterenol, the ventricular rate was recorded at 12 per minute and his condition deteriorated. An external pacemaker was applied with a stimulating rate of 40

From the Department of Thoracic Surgery, University of Pittsburgh, Pittsburgh, Pa.

Read at the Fortieth Annual Meeting of The American Association for Thoracic Surgery at Miami Beach, Fla., May 11-13, 1960.

shocks per minute at 52 volts and immediate improvement was noted. At the end of 3 days it was necessary to raise the pacemaker voltage to 70, since lower values elicited a two to one response (Fig. 1). The intrinsic rate varied between 10 to 16 per minute.

Attempts to maintain the pacemaker on a standby basis were unsuccessful and resulted shortly in Stokes-Adams seizures. Over the next 4 weeks the patient's response to the external pacemaker was characterized by an increased threshold to stimuli. Progressively higher voltages were required to maintain an adequate cardiac rate. Steroids were administered without evident improvement. Convulsive episodes now occurred whenever the pacemaker was momentarily discontinued. It was estimated that he had suffered over 200 seizures. He was subsequently transferred to this hospital, a distance of 130 miles, on an external pacemaker with a mobile power supply.

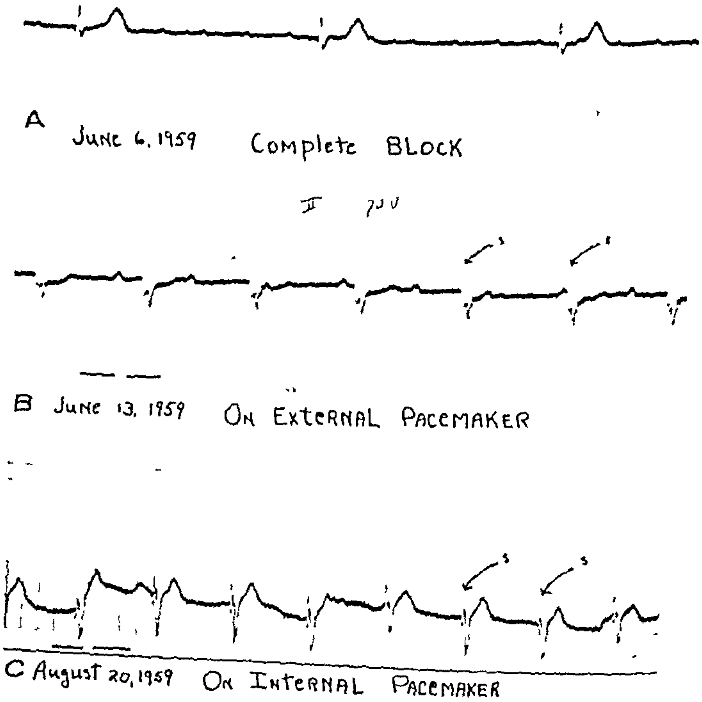


Fig. 1.—Preoperative (*A* and *B*) and postoperative electrocardiograms (*C*) in Case 1 (H. S.). Internal and external pacemaker impulses are indicated by a vertical line preceding the ventricular complex.

The patient had been externally paced for 55 days. Physical examination showed a blood pressure of 150/80 mm. Hg with an imposed pulse rate of 40 per minute. He appeared well adjusted to the frequent contractions of his chest muscles on the left side and was alert and cooperative. His skin showed pigmentation and second degree electrical burns on the anterior and posterior chest wall where the stimulating electrodes had been applied (Fig. 2). Two small ulcers in the same area were secondarily infected. The muscles of the left hemithorax were hypertrophied and contracted at a rate of 40 per minute. The patient breathed shallowly and synchronously with the pacemaker impulses. The lungs were clear. Because of the constant movement of the patient's chest, it was not possible adequately to examine the heart. Aside from a 3+ enlargement of the prostate, the remainder of the physical examination was not remarkable. Routine laboratory studies were within normal limits. It was elected to convert the patient from an external pacemaker, which had sustained him for 58 days, to a direct myocardial stimulating unit.

On Aug. 3, 1959, under light Pentothal and nitrous oxide anesthesia supplemented by succinylcholine, a left anterior thoracotomy was performed through the fourth intercostal space. Muscle contractions ceased following the administration of the muscle relaxant while the heart continued to respond to stimuli from the external pacemaker. The stimulating and indifferent electrodes, incorporated in a nonconductive, Silastic (Dow-Corning) patch, were embedded into the myocardium of the left ventricle and fixed to the epicardium with interrupted silk sutures. The Teflon-Silastic insulated leads were secured to a rib and brought out through the left anterior chest wall. These were connected to the transistorized pacemaker and a pulse rate of 70 per minute was established as the external pacemaker was discontinued. Direct observation of the heart, blood pressure, and the electrocardiogram confirmed the effectiveness of the new impulse (Fig. 1). At the conclusion of the procedure, the patient's blood pressure was 130/80 mm. Hg and he reacted promptly. As a safeguard against equipment or patient failure, the external pacemaker was placed on a standby monitoring circuit triggered to respond to an asystolic interval of 6 seconds.[4]

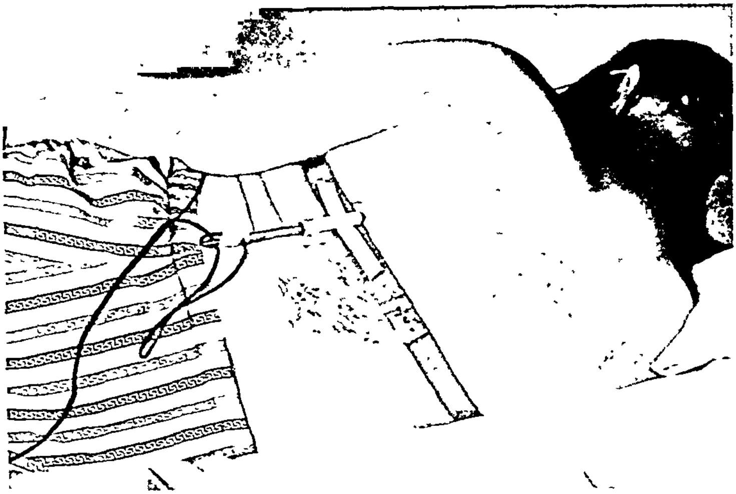


Fig. 2.—Cutaneous pigmentation and ulceration beneath one of the electrodes of the external pacemaker after 55 days of almost continuous use in Case 1.

On the first postoperative day, asystole occurred which was managed by the external pacemaker. Thereafter, his blood pressure fell to 70/40 mm. Hg and he appeared in shock. Increasing frequency of dropped beats was observed in response to pacemaker stimuli. Maximum currents failed to alter the cardiac function and for 6 hours the patient remained in precarious condition. Intravenous sixth molar sodium lactate together with metaraminol produced dramatic improvement. Ventricular contractions became synchronous with pacemaker impulses and the blood pressure rose to 140/80 mm. Hg. For the next 8 days the patient required intravenous metaraminol to combat frequent episodes of hypotension associated with profuse diaphoresis. He received no lactate during this period. Oliguria occurred on the third postoperative day which persisted for 3 days. By the ninth postoperative day he was on substantial oral intake and his general condition appeared satisfactory. The metaraminol infusion was progressively diminished and discontinued on the fifteenth postoperative day. At this time a left pleural effusion, consisting of 1,500 ml. of serosanguineous fluid, was evacuated, which was sterile to culture.

A coagulase-positive, staphylococcal infection, attributed to a wound infection at the site of the external electrodes, developed along the thoracotomy tube drainage tract and around the sinus tract occupied by the electrode cable. These cleared somewhat under intensive local care and antibiotic therapy.

On the twenty-seventh postoperative day, 8 hours following a "dry" chest tap, the patient suddenly collapsed while walking in his room. He appeared in profound shock. The pacemaker was functioning satisfactorily. Vasopressors failed to improve his condition. For the first time the patient complained of abdominal pain and examination revealed generalized tenderness and rebound with absent bowel sounds. An abdominal catastrophe was suspected and a peritoneal tap returned grossly bloody fluid. Following transfusion of 3,500 ml. of blood, laporotomy was performed for massive intraperitoneal hemorrhage of undetermined origin. A ruptured subcapsular hematoma on the costal surface of the spleen was found which was bleeding actively. Splenectomy was performed and the abdomen cl[illegible]. During the procedure which proceeded uneventfully, the internal pacemaker was main[illegible] at a rate of 80 per minute to compensate for the high output demand. Although no [illegible] perforation of the left hemidiaphragm was detected, the unsuccessful thoracentesis was [illegible] implicated as the precipitating factor.

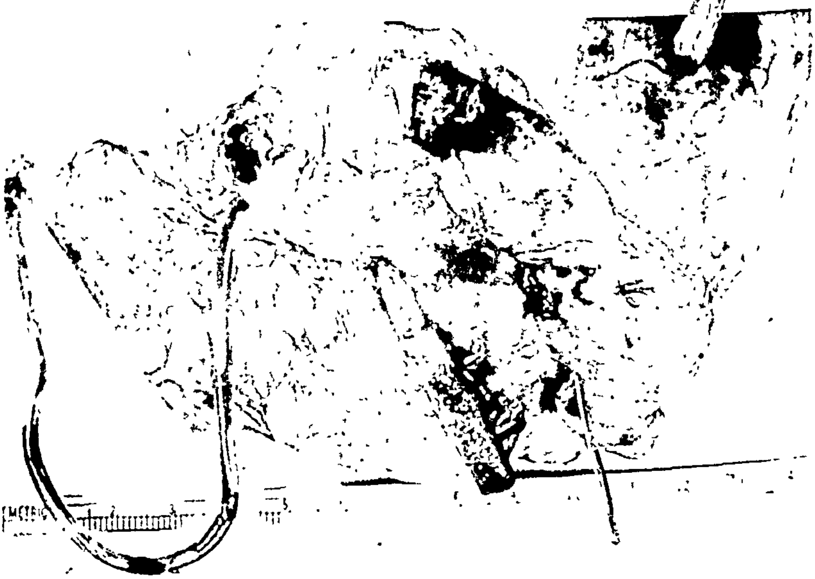


Fig. 3.—Postmortem appearance of the heart in Case 1 demonstrating probe in the perforation at base of abscess in the apical portion of the left ventricle and the displaced bipolar electrode.

The patient's postoperative course was relatively uneventful. Metaraminol was required for 48 hours and then discontinued. Irregularly skipped beats accompanied by mild hypotension were noted on the ninth day after splenectomy, 6 weeks after electrode implantation. This deficit between the imposed rate and the patient's pulse was corrected by increasing the current to 15 Ma. There was continued drainage about the pacemaker cable and from the site of the thoracotomy drainage tube. The patient was discharged 13 days after splenectomy, afebrile, with the pacemaker set at a rate of 70 per minute.

While at home the patient was able to care for his needs, walk without assistance, and engage in limited activities. Aside from battery changes every 25 days, no pacemaker adjustments were required until the eighth week following discharge, when dropped beats were again recorded. These increased over the next 3 days despite maximum current settings. The pulse rate fell to 20 per minute and he experienced many syncopal attacks and convulsive seizures. Electrocardiograms showed complete absence of a ventricular response to internal pacemaker stimuli and he was placed on an external pacemaker. The patient's condition improved as his heart rate increased. Twenty-four hours later, on Nov. 11, 1959, he suddenly died, after having been continuously sustained by direct myocardial stimulation for slightly over 3 months.

At postmortem examination, the pacemaker leads were seen to traverse a sinus tract containing a moderate amount of purulent material. They joined the electrode patch which was displaced to one side and was not in contact with the epicardium of the left ventricle. Surrounding the patch was an irregular abscess cavity containing purulent fluid, which extended through the entire thickness of the apical portion of the left ventricle (Fig. 3). The muscle bordering the perforation was ragged and necrotic. Considerable hemorrhage was noted covering the surface of the heart and in the remainder of the mediastinum. Advanced atherosclerosis involving both the anterior descending and circumflex branches of the left coronary artery was noted. The left pleural cavity contained a loculated subparietal abscess which did not appear to communicate with the sinus tract or the myocardial abscess. Death was attributed to ventricular rupture secondary to abscess formation.

Comment: Infection along the tract created by the electrode cable was responsible for the fatal outcome in this patient. It is recognized that the transthoracic leads can function as a wick inviting bacterial contamination of the thoracic viscera. It is of interest that the septic foci just described failed to produce the usual clinical manifestations, doubtless because of the intensive antibiotic therapy which the patient received during his hospitalization.

CASE 2.—B. V. was a 71-year-old white man who was first seen at the Presbyterian Hospital in February, 1959, for treatment of an anaplastic carcinoma of the bladder. A routine electrocardiogram at that time showed a first degree heart block and a right bundle branch block. Repeat electrocardiograms in September, 1959, disclosed a second degree heart block and a left bundle branch block (Fig. 4). While in the hospital for urologic studies, he had a sudden syncopal episode associated with rigidity of his extremities which lasted for 10 seconds. At this time, examination revealed a cardiac rate of 30 per minute and the electrocardiogram showed a complete heart block (Fig. 4). Isoproterenol was administered sublingually, 20 mg. every 6 hours, and a cardiac rate of 40 per minute was established over the next 24 hours. He was discharged one week later, asymptomatic but still in complete heart block.

On Oct. 21, 1959, he was readmitted because of some six to eight syncopal episodes suffered in the previous 3 days. Examination disclosed a blood pressure of 115/50 mm. Hg and a regular radial pulse of 32 per minute. The lungs were clear save for bilateral inspiratory râles at both bases which cleared on coughing. Clinical examination showed that the heart was not enlarged. The second sound was loudest at the pulmonic area and a harsh Grade 2 systolic murmur was present at the base with transmission into the neck. Varying intensity of the first heart sound and a protodiastolic gallop were noted. No organomegaly was noted on abdominal examination. There was no peripheral edema. The electrocardiogram showed complete atrioventricular dissociation with an auricular rate of 104 and a ventricular rate of 32. The QRS pattern was that of a right bundle branch block. Transverse enlargement of the cardiac silhouette with a left ventricular contour was noted on a chest roentgenogram.

Following admission, the patient was connected to an external pacemaker which was placed on a standby monitoring circuit and set for an asystolic interval in excess of 6 seconds. Isoproterenol was increased to 10 mg., sublingually, every 6 hours. During the course of the next 3 days, the average pulse rate was 40 per minute. Despite an increase in the dose of isoproterenol to 12.5 mg. every 2 hours, he had frequent episodes of asystole lasting from 2 seconds to a period of time sufficient to activate the external pacemaker. The majority of these attacks occurred while the patient was asleep at night.

On Oct. 26, 1959, an anterior thoracotomy was performed through the fourth left intercostal space and direct myocardial stimulating electrodes were implanted into the left ventricle, as in Case 1. The current was increased to 3 Ma., at which point the myocardium responded to each impulse of the internal pacemaker at a rate of 80 per minute with no dropped beats (Fig. 4).

The immediate postoperative course was complicated by unexplained hypotension. The patient's blood pressure ranged between 80/60 to 100/70 mm. Hg. After 24 hours, this stabilized at preoperative levels without therapy. Serum electrolytes on the first postoperative day revealed a moderate hyponatremia which was gradually corrected by specific fluid therapy. By the seventh postoperative day he was on substantial oral feedings and the electrolyte values were within normal limits. During the entire period following operation, the pacemaker was maintained at 3 Ma. and at a rate of 70 to 80 per minute. No evidence of dysfunction or further syncopal episodes were observed. The patient was discharged on the sixteenth postoperative day on no medication.

One month after discharge the patient was readmitted with a one-week history of frequent syncopal attacks. In addition, he had noted dyspnea on exertion, orthopnea, and ankle edema. Examination revealed a complete atrioventricular block with an apical rate of 32 per minute. Fine inspiratory râles were noted at both lung bases and 3+ pitting edema of the ankles was present. Substitution of an alternate pacemaker resulted in an immediate response at 4 Ma. Digitalis and diuretic therapy were instituted, in addition, and marked improvement in the signs and symptoms of congestive failure were noted within 48 hours. A defect was subsequently found in the original transistorized pacemaker.

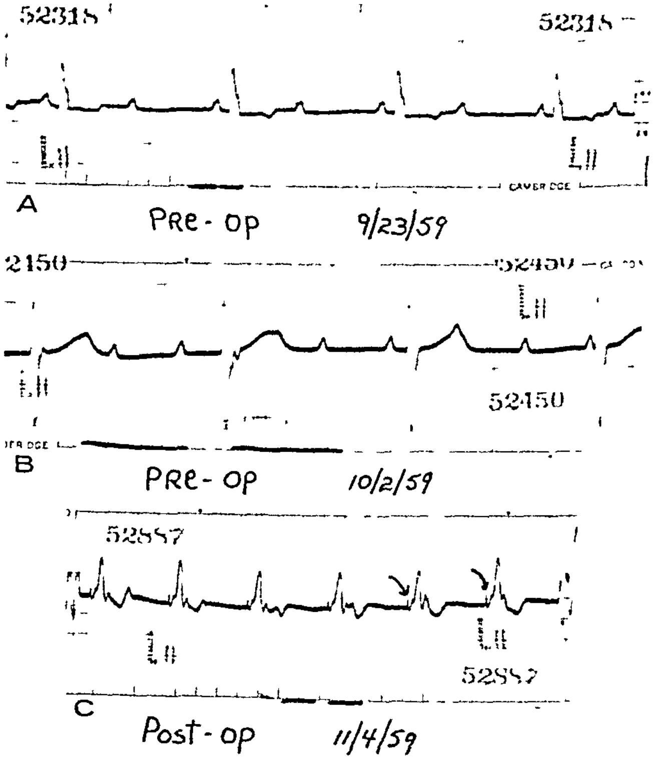
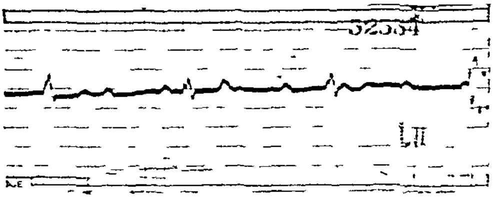


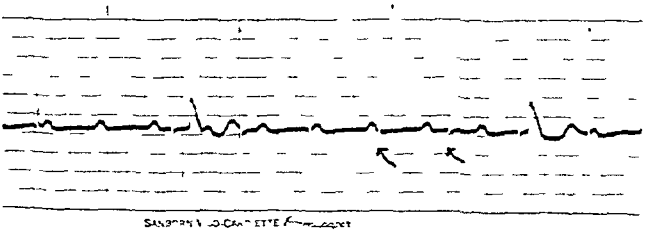
Fig 4.—Electrocardiogram of Case 2 (B. V.) which shows partial A-V block with a left bundle branch block (*A*), and a complete A-V block (*B*), and the patient on the internal pacemaker (*C*). Impulses are indicated by vertical lines preceding ventricular complexes

During the 7 months since discharge, he has remained asymptomatic and has been able to engage in limited activities. The current from the present apparatus has been gradually raised to 6 Ma. with the finding of occasional dropped beats. The only other complication has been persistent purulent drainage from around the electrodes entering the chest wall.

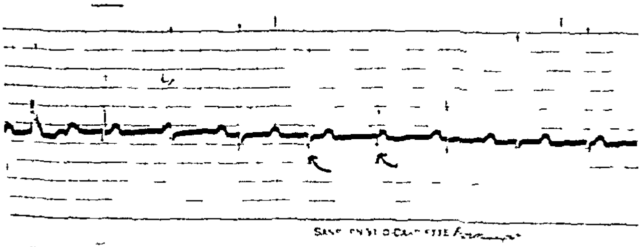
Case 3.—O. W. was a 57-year-old white man, a retired coal miner, who was admitted to this hospital on Oct. 8, 1959, with a history of frequent syncopal attacks during the preceding 5 months. He had been relatively well, except for mildly progressive dyspnea on exertion, until 5 months prior to admission when he experienced a sudden loss of consciousness, lasting approximately 20 seconds, which was accompanied by a clonic convulsion. Subsequently, he noted considerable shortness of breath on exertion and at rest. Persistent substernal pain occasioned his admission to the local hospital for possible myocardial infarction. At this time he appeared dyspneic. Loud expiratory wheezes were exhibited throughout both lung fields with prolongation of this phase of respiration. An electrocardiogram showed a complete heart block with an atrial rate of 65 and a ventricular rate of 40. He responded well to digitalis and diuretic therapy and was discharged. However, syncopal attacks slowly increased in frequency, as many as four occurring daily. The patient had recorded his pulse on these occasions and noted that it varied from 30 to 40 per minute. A definite increase in dyspnea was experienced with rates below 36 per minute.



A ON ADMISSION



B BROKEN ELECTRODE



C INCREASING ASYSTOLIC INTERVAL

Fig 5A.—Electrocardiogram in Case 3 (O W.) which shows complete A-V block (*A*), failure of imposed impulse to stimulate a ventricular complex with reappearance of an idioventricular rhythm on the seventeenth postoperative day (*B*), and impending ventricular asystole (*C*). Shortly thereafter, thoracotomy and cardiac massage were performed for ventricular standstill Pacemaker impulses are indicated by vertical lines.

Examination revealed a blood pressure of 170/70 mm. Hg and a regular pulse of 44 per minute. No venous distention was noted. The lungs were clear except for a prolonged expiratory phase. The heart was moderately enlarged. The second sound was loudest in the pulmonic area. There was marked variation in the intensity of the first heart sound; audible atrial contractions were detected at the apex. The liver was enlarged to 7 cm. below the right costal margin. Minimal pretibial and ankle edema was present. Admission laboratory studies were within normal limits except for a urinary protein of 250 mg. per cent. Electrocardiogram confirmed the presence of complete atrioventricular dissociation (Fig. 5*A*).

The QRS complexes had the contour of a right bundle branch block. Chest x-ray studies disclosed a moderate degree of pulmonary congestion and cardiomegaly with predominantly left ventricular enlargement.

Under continued digitalization, bed rest, and mercurial diuresis, an eight pound weight loss was effected with subjective improvement and a decrease in the signs of congestive heart failure. Isoproterenol, 10 mg. every 6 hours sublingually, was administered on admission and increased to 10 mg. every 2 hours as the need arose. Despite these measures, he experienced multiple syncopal episodes and convulsive seizures. Two days later, some 20 attacks were recorded in a 24-hour period; isoproterenol administered sublingually, had seemingly little effect. Sixth molar sodium lactate was then administered by slow intravenous drip and the ventricular rate stabilized at 40 to 50 per minute with cessation of the asystolic periods. In view of the difficulties encountered in controlling the patient's cardiac rate, it was elected to implant direct stimulating myocardial electrodes.

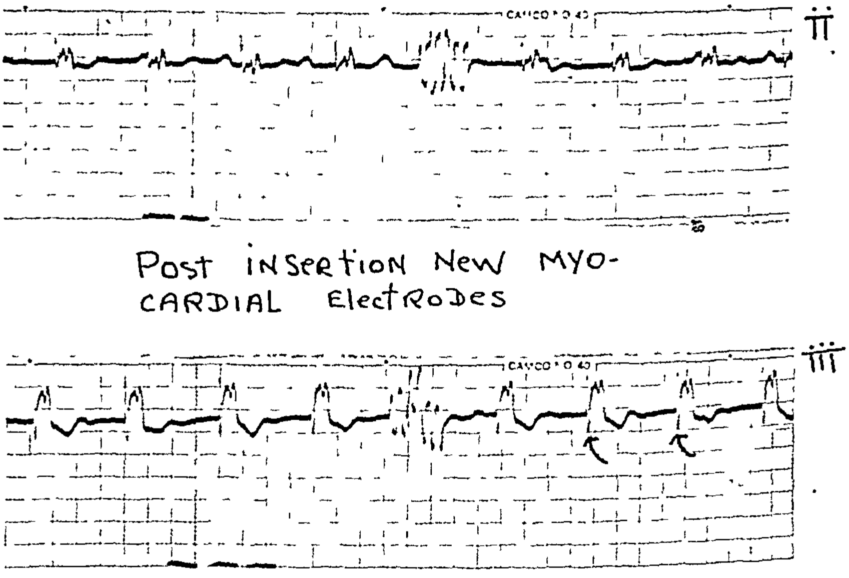


Fig. 5B.—Postoperative electrocardiogram in Case 3 which shows regularly paced QRS complexes immediately preceded by the vertical line of the imposed impulse.

On Oct. 13, 1959, an anterior thoracotomy was performed through the left fourth intercostal space and two polyethylene insulated, No. 2-0, multifilament, stainless steel wires were deeply anchored into the myocardium approximately 2 cm. apart. A single suture of No. 3-0 silk was used to fix the polyethylene tubing to the epicardium. The myocardium responded to a stimulus of 6 Ma. and was paced at a rate of 80 per minute.

The postoperative recovery was uneventful and by the end of the first week exercise tolerance exceeded preoperative levels. Increasing numbers of dropped beats were noted from the first postoperative day, however, and the current requirement was gradually increased until the maximum output of the pacemaker was attained. On the seventeenth postoperative day, the patient suddenly complained of dizziness and a pulse rate of 30 per minute was recorded. The electrocardiogram showed a reversion to an idioventricular rhythm with no response to the stimulus provided by the pacemaker (Fig. 5A). The pulse rate slowed rapidly and complete asystole occurred. An external pacemaker was applied but no response could be elicited at maximum voltage. After approximately one minute of asystole, emergency thoracotomy was performed on the ward and cardiac massage instituted. Ventricular contractions reappeared at a rate of 30 per minute. Sixth molar sodium lactate was administered intravenously and the cardiac rate rose to 45 per minute. The patient was brought to the operating room and the left thorax was explored after extension of the previous incision. Pericardial and pleural adhesions prevented dissection and exposure of the stimulating electrodes to ascertain the cause of the dissociation between pacemaker impulse and myocardial response. A second pair of electrodes, similar to the first implant, was fixed to the myocardium in identical fashion. Stimulation of the ventricles was achieved at a current of 3 Ma. (Fig. 5*B*).

Postoperatively, the patient's uneventful recovery was marred only by a superficial wound infection. At the time of discharge, 28 days following the second implant, the heart was paced at 5 Ma. at a rate of 64 per minute without dropped beats.

The patient was readmitted 2 months later, on Jan. 23, 1960, because of an erratic response to the pacemaker. The difficulty was ascribed to the transistorized unit; substitution of an alternate pacemaker resulted in a satisfactory myocardial response at 10 Ma. The appearance of an idioventricular rhythm on March 10, 1960, prompted his readmission. Attempts to establish a ventricular response to the pacemaker were unsuccessful. After eliminating the factor of pacemaker dysfunction, it was determined that effective electrical contact was no longer present between the electrodes and the myocardium. The patient had done well despite the lack of artificial pacing. With an idioventricular rate stabilized at 40 per minute, he suffered no syncopal attacks and only a mild increase in exertional dyspnea. He was subsequently discharged on full doses of isoproterenol. A persistent purulent drainage is present about the leads at site of exit from the chest wall but the patient has declined removal of these wires at this time.

Comment: Either extrusion from the myocardium, rupture of the wire leads, or short circuiting because of dissolution and loosening of the polyethylene insulation could account for the failure of this type of implant to function for longer periods. As a result of this experience, we have favored the nonconductive, bipolar, patch electrode for direct-myocardial stimulation.

DISCUSSION

The vital functions of patients with complete heart block and extended or recurrent periods of asystole are jeopardized by circulatory insufficiency. Prompt and sustained application of the external pacemaker under these conditions may be lifesaving, as was demonstrated in the first patient who was maintained in this fashion for 58 days. It was noteworthy that there were no pathological changes in the heart or surrounding mediastinal structures, detected either at operation or postmortem examination, which could be directly attributed to prolonged use of the external unit. However, Reiff and his associates[5] have reported pericardial and epicardial hemorrhages in a patient who had been externally paced for 24 hours. Electrical burns, muscular spasms, and high pacing voltages limit the patient's tolerance to continuous use of this form of treatment. Some patients require temporary support by the external pacemaker for Stokes-Adams attacks occurring at the onset of or during complete heart block and then revert permanently to an adequate ventricular rhythm. In the presence of a persistently slow rate, intermittent use of the external pacemaker for sporadic attacks is associated with a high mortality.[1, 2] This is ascribed to ventricular standstill during an unpaced interval, which is the principal reason for sudden death in established complete atrioventricular block.[6]

In the older patient, the most common cause of complete heart block is coronary artery disease. This may occur following an acute occlusion or as a result of progressive myocardial ischemia which is due to coronary atherosclerosis. The nature of the organic lesion and its contribution to the surgical risk temper the choice of an operative approach to the treatment of complete heart block. In addition, consideration of surgical therapy implies failure to respond to an intensive program of medical management including sympathomimetric amines, parasypatholytic agents, and steroids.

The selection of patients for implantation of direct stimulating electrodes has been primarily based upon the incidence of Stokes-Adams seizures associated with depressed idioventricular rates. Although the reported experience is limited and our own series small, it has been possible to define several clinical situations wherein this procedure may be clearly indicated. In one group of patients, a chronic state of circulatory insufficiency prevails, attended by frequent syncopal and convulsive paroxysms. The ventricular rate is extremely low, usually less than 20 per minute. When acceleration cannot be achieved under a medical regimen, emergency support should be provided by an external pacemaker. Conversion to an internal pacemaker is indicated where there is continued failure to revert to an adequate rhythm. In another category are patients with third degree block, who, over a period of months or years, demonstrate progressive ventricular slowing to rates ranging between 20 to 40 per minute. Initially well compensated, they experience insufficiency during exercise because of an inability to accelerate in response to a need for greater peripheral blood flow. Dizziness and weakness are succeeded by frequent attacks of syncope at rest, associated with periods of ventricular asystole. Prolongation of the asystolic interval precipitates a convulsive episode which may be accentuated by the presence of cerebral arteriosclerosis. Since these patients experience intermittent bouts of reduced cardiac output over an extended period, they are difficult to control with an external pacemaker. It appears that in these cases the direct stimulating electrode enjoys its widest applicability.

Effective circulation may be maintained at fixed ventricular rates as slow as 20 to 30 per minute. This is accomplished through prolongation of diastole, greater ventricular filling, and increased stroke output. A persistent heart block ultimately promotes ventricular dilatation because of the constant requirement for an increased stroke volume. In a heart already impaired by coronary insufficiency, dilatation will produce a further reduction in the cardiac reserve. Eventually, congestive failure supervenes and is not an uncommon cause of death in complete heart block.[6] It is suggested that these events may be reversed by pacing the heart, at an optimum rate, thereby shortening the cardiac cycle, reducing the diastolic filling time and improving the cardiac output. Although experimental evidence is lacking, clinical observations appear to support the contention that the cardiac output of the paced heart is augmented. When the pacemaker was discontinued and a slow idioventricular rate prevailed for 5 or 6 days or more, the signs of congestive failure were noted (Cases 2 and 3); improvement occurred after pacing was restored. Experimental studies comparing the cardiac output of the completely blocked and the paced heart are being conducted and will be presented in a separate paper.

The preoperative preparation of these patients was principally directed toward the treatment of congestive heart failure. Accordingly, digitalis was administered for the usual indications. Despite the absence of normal cardioacceleration, vital signs were maintained without difficulty throughout all three procedures. In a similar experience, Penton and his associates[6] reported no mortality in 24 major operations in 19 patients with complete heart block.

The bipolar electrode* which was used in 2 of the patients consisted of a 2.5 by 1.5 by 0.5 cm. nonconductive patch of Silastic in which were incorporated the stainless steel prongs of the stimulating and indifferent electrodes, separated by a distance of 1.2 cm. These were embedded into the myocardium of either the right or left ventricles, and fixed to the epicardium by four to six interrupted silk sutures. Care was taken to avoid grossly infarcted areas and coronary vessels. The stainless steel leads were insulated by Teflon and Silastic and were connected to a light weight (10 ounces) transitorized unit,* utilizing 9-volt mercury batteries and delivering a current up to 25 Ma. (Fig. 6). The stimulus was approximately 2 msec. in duration with a square wave contour. With this apparatus, pacing rates could be varied from 50 to 200 impulses per minute. Batteries were changed every 25 days. Placement of the indifferent electrode adjacent to the stimulating electrode rather than at a distance, that is, the chest wall, has produced less myocardial fibrosis about the stimulating electrode. As a consequence, tissue resistance and the current required for impulse formation were reduced. In practice, initially low milliamperage settings (2 to 3 Ma.) were gradually increased over a period of 3 to 8 weeks. The appearance of frequent dropped beats signalled the need for higher current adjustments. Thereafter,

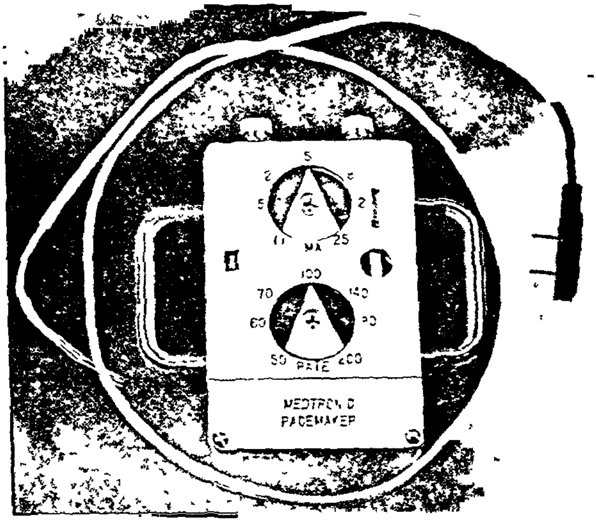


Fig. 6.—Bipolar patch with stainless steel prongs of indifferent and stimulating electrode and transistorized pacemaker unit.

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*Manufactured by Medtronic, Minneapolis, Minn.

current requirements generally remained constant at 5 to 15 Ma. with the rate maintained at 60 to 70 per minute.

Clinical and experimental studies have emphasized the close relationship between blood pH and the cardiac mechanism. Bellet and his associates[7] showed that the administration of a molar sodium lactate solution enhanced the rhythmicity of the heart in complete block. Acceleration of the heart rate was attributed to increased myocardial excitability due to elevation of the pH. It has also been demonstrated that acidosis of metabolic or respiratory origin diminished the inotropic response of the heart to sympathomimetic amines whereas alkalosis potentiated this effect.[8-11] These observations suggested an explanation for the changes occurring in the immediate postoperative period in the first case, which were characterized by hypotension, a falling pulse rate, and the lack of correspondence between the imposed impulse and the ventricular complex. Although pH determinations were not available, it was reasonable to assume that postoperative metabolic acidosis and respiratory acidosis, secondary to ventilatory insufficiency, prevailed. Under these circumstances, reduced myocardial contractility, accompanied by a lowered stroke volume and cardiac output, resulted in hypotension. Similarly, an increased threshold of ventricular excitability was attended by decreased responsiveness to external electrical stimuli and accounted for the impulse deficit. It appeared that reversal of these effects of acidemia was brought about by the administration of sixth molar sodium lactate in conjunction with a sympathomimetic amine, in this case metaraminol. Once the response to pacemaker stimuli was reestablished, it was possible to maintain the blood pressure at near normal levels with a vasopressor until it became stabilized. On two occasions in Case 3, acceleration of a slow, non-sustaining idioventricular rate was obtained by the administration of sixth molar sodium lactate.

Infection about the leads exiting from the chest wall has constituted a serious problem. In all 3 cases, coagulase-positive staphylococcus has been isolated from the sinus tract at one time or another and has resisted intensive local and systemic antibiotic treatment. The potential hazard of contamination of the underlying mediastinal structures was realized in the first patient, 3 months postoperatively, with a fatal issue. The remaining patients have been followed for 7 months and have shown no signs of developing this distressing complication. Remote radiofrequency excitation of a miniature intracorporeal receiver, with wires leading to the myocardium, has been proposed to eliminate the need for a transthoracic cable.[12]

Other methods, which avoid entering the pleural cavity, have been described to directly stimulate the myocardium. The intravascular electrode of Furman,[13, 14] introduced through a peripheral vein, stimulates the endocardial surface of the right ventricle; continuous anticoagulation is needed to prevent clotting about the tip of the electrode. Myocardial electrodes implanted percutaneously[15, 16] may injure the coronary vessels and are subject to spontaneous displacement. While successful clinical application of these techniques for short intervals have been recorded, the long-term results in continuously paced subjects are not yet available.

The therapeutic value of repetitive electrical stimuli, directly applied to the heart in complete block, has been well established. Final evaluation of the technique described for placement of myocardial electrodes must await further clinical trials.

SUMMARY

1. Direct stimulation of the heart through an implanted bipolar myocardial electrode has been reported in 3 cases of acquired atrioventricular block associated with Stokes-Adams seizures. These patients had failed to respond to an extended trial of medical management in conjunction with an external pacemaker.

2. The advantages of the bipolar patch electrode have been described together with the details of operation of the transistorized pacemaker.

3. In the immediate postoperative period, the use of sixth molar sodium lactate and the sympathomimetic amines to combat hypotension and the apparent refractoriness of the ventricular myocardium to the imposed impulse is recommended.

4. The problem of infection, introduced through the transthoracic cable, which was responsible for the death of one of these patients, has been discussed.

The authors wish to express their appreciation to Dr. Jesse Jenkins, of the Fairmont General Hospital, Fairmont, West Virginia, for his assistance in the treatment of Cases 1 and 3 and for securing the pathologic material described herein.

REFERENCES

1. Zoll, P. M.: Resuscitation of the Heart in Ventricular Standstill by External Electrical Stimulation, New England J. Med. 247: 768, 1952.
2. Zoll, P. M., Linenthal, A. J., Leona, R. N., and Belgard, A. H.: Treatment of Stokes-Adams Disease by External Electric Stimulation of the Heart, Circulation 9: 482, 1954.
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4. Zoll, P. M., Linenthal, A. J., Norman, L. R., Paul, M. H., and Gibson, W.: Treatment of Unexpected Cardiac Arrest by External Electric Stimulation of the Heart, New England J. Med. 254: 541, 1956.
5. Reiff, T. R., Oppenheimer, J., and Ferguson, G.: Cardiac Injury Presumably Due to Use of the External Cardiac Pacemaker in Stokes-Adams Disease, Am. Heart J. 54: 437, 1957.
6. Penton, G. B., Miller, H., and Levine, S.: Some Clinical Features of Complete Heart Block, Circulation 13: 801, 1956.
7. Bellet, S., Wasserman, F., and Brody, J. I.: Effect of Molar Sodium Lactate in Increasing Cardiac Rhythmicity, Tr. A. Am. Physicians 68: 161, 1955.
8. Campbell, G. S., Houle, D. B., Crisp, N. W., Jr., Weil, M. H., and Brown, E. B., Jr.: Depressed Response to Intravenous Sympathomimetic Agents in Humans During Acidosis, Dis. Chest 33: 18, 1958.
9. Thrower, W. B., Darby, T. D., Aldinger, E. E., Tenney, J. M., and Westbrook, S. H.: Studies of the Relationship Between Sympathoadrenal Function Acid Base Derangements and Ventricular Contractile Force, Surgical Forum, 45th Clinical Congress, Atlantic City, 1959.
10. Nahas, G. B., and Ligou, J. C.: Effects and Acute Arterial Blood pH Changes on Catecholamine Plasma Levels and Circulatory Adaptations, Surgical Forum, 45th Clinical Congress, Atlantic City, 1959.
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11. Keith, H. B., Snyder, D. D., and Campbell, G. S.: Cardiac Output and Pressor Response Changes Before, During, and After Metabolic Acidosis, Tr. Am. Soc. Artificial Int. Organs, Chicago, 1960.

12. Glenn, W. W. L., Mauro, A., Longo, E., Lavietes, P. H., and Mackay, F. S.: Remote Stimulation of the Heart by Radiofrequency Transmission, New England J. Med 261: 948, 1959.
13. Furman, S., and Robinson, G.: The Use of an Intracardial Pacemaker in the Correction of Total Block, Surgical Forum, 44th Clinical Congress, Chicago, 1958
14. Furman, S., and Schwedel, J. B.: An Intracardiac Pacemaker for Stokes Adams Seizure, New England J. Med. 261: 943, 1959.
15. Thevenet, A., Hodges, P. C., and Lillehei, C. W.: The Use of the Myocardial Electrode Inserted Percutaneously for Control of Complete Atrioventricular Block by an Artificial Pacemaker, Dis. Chest 34: 621, 1958.
16. Ross, J. K., and Harkins, G. A.: Percutaneous Introduction of Cardiac Pacemaker Electrode, Lancet 2: 1109, 1959.

Discussion

DR. ELLIOTT S. HURWITT, New York, N. Y.—This is an interesting and courageous approach to the problem of heart block. There are, however, several disadvantages to this method, including anesthesia, thoracotomy, the use of electrodes which may fatigue and break, and the development of fibrosis around the myocardial electrode, necessitating frequent increases in the amplitude of current in order to maintain an effective stimulus

All of these problems may be circumvented by employing an endocardial pacemaker, in which the effective electrode, a conductive wire contained in a cardiac catheter introduced through a peripheral vein, delivers its impulse in contact with the endocardial surface of the right ventricle. This technique, developed in our own laboratory and clinically by Dr. Seymour Furman, surgical resident at the Montefiore Hospital and presented by him at the Forum of the American College of Surgeons in 1958, has been applied by our group to 18 patients to date. The classical picture of Stokes Adams attacks was the presenting problem in 16 of these, from 48 to 81 years of age; the atrioventricular dissociation in the oldest occurred in the course of a fresh myocardial infarct, with a successful outcome

The people are maintained on an ambulatory outpatient basis, on anticoagulant therapy, and some have returned to full activity while the endocardial electrode is still in place, powered by a small, portable, battery operated transistorized pacemaker. There has been no need to increase the amplitude of the small current in any patient, despite many months of continuous or intermittent stimulation.

Of particular interest to this meeting are 2 children, aged 2 and 5 years, with surgically produced heart block following the open correction of septal defects Both of these children had become refractory to the myocardial wires placed at the time of surgery, and both were then paced successfully by the endocardial technique, death was ultimately due to causes other than the consequences of heart block

DR WILLIAM L. WEIRICH, Minneapolis, Minn.—This report certainly points up some of the problems with which this method is plagued

I would like to illustrate our experience with just 1 case—a 37 year old man with congenital complete heart block, who was asymptomatic until 2 years prior to the time that we saw him when he had a cardiac arrest while folk dancing.

He had about fifty bouts of momentary cardiac arrest lasting from 1 to 41 seconds Nine months ago we implanted a bipolar electrode exactly like the one you saw on the screen Four months following operation, he returned to work, he is now working 6 days a week, 6 hours a day, as a tool and diemaker, and with a rate maintained between 76 and 81.

He is relatively asymptomatic. We have had the problem of having to change the pacemaker on two occasions, because of defects in the components. Within the first 3 weeks following implantation, the current demands to stimulate the heart increased rapidly. However, since that time we haven't had to increase it more than 2 milliamperes

The first slide shows the gross cardiomegaly. This patient was catheterized, and showed no evidence of a septal defect. The electrocardiogram demonstrated left as well as right hypertrophy.

This slide shows the heart size 8 months following implantation of the electrode, and artificial control of the heartbeat at approximately 80 a minute. There has been a significant reduction in size.

I certainly don't think this is a panacea for this type of arrhythmia, and the optimum treatment will probably be oral medication. However, it is a satisfactory method of keeping these patients alive and allows them to lead useful lives.

DR. HARVEY J. MENDELSOHN, Cleveland, Ohio.—We anticipated some of the difficulties that Dr. Levowitz has had and, being presented with problems in 2 patients who had typical Stokes-Adams syndromes with repeated episodes of syncope and, who had failed to respond to treatment by the usual methods, including steroids, we decided to try a different approach.

The first patient was a 60-year-old man, and we chose to approach this from the vagal reflex aspect. This man had a small hiatus hernia. However, we could not prove by stimulation that this was the cause of triggering his mechanism. In this individual, arteriosclerosis, I'm sure, was a primary factor in the repeated Stokes-Adams syncope.

We first repaired the hiatus hernia. At the same time we sectioned the vagus nerve just inferior to the recurrent nerve on the left. The man had a period of improvement for a few months, but he still required Isuprel and atropine.

About 9 months later we sectioned the right vagus nerve transthoracically paratracheally. Since then this man has got along with a bradycardia and with no further syncopal attacks for 2½ years. He has been able to work effectively.

The second patient was a woman with sarcoidosis in her late thirties. Steroids were ineffective, and she was threatened with decerebration because of repeated episodes of heart block and hypotension.

In this case we chose to do a vagectomy inferior to the left recurrent nerve through the left chest. At the same time we resected a portion of the right vagus paratracheally.

This patient has not done well. She is living 2 years later but with recent episodes of heart block and hypotension. We believe there are a certain number of patients in whom the long-term use of electrodes can be obviated. The prolonged use of implanted electrodes is not an appealing method for a person who has a continuing disease and the problem of infection will always exist.

DR. WILLIAM B. FORD, Pittsburgh, Pa.—The use of direct myocardial electrodes with a transistorized pacemaker is an acceptable procedure. The operation is simple, as compared to other thoracic surgical procedures, and the complications that arise usually can be controlled. However, one should not use the monofilament wire, for this wire breaks when it is used as a myocardial electrode. Rather, the bipolar electrode, such as was developed by Dr. Hunter in Minneapolis, is suggested.

This procedure is, therefore, recommended for patients having Stokes-Adams seizures with a complete heart block, when they are not controlled with good medical management.

DR. LEVOWITZ (Closing).—I wish to thank the various discussers for their remarks. One of the disadvantages of the myocardial electrode is the transthoracic cable. Elimination of the percutaneous lead would be most desirable. Dr. Glenn and his associates have reported on the clinical use of an intracorporeal receiver which is activated by a remote radio frequency transmitter. This technique appears promising and is currently being studied in our laboratory.

SURGICAL CORRECTION OF TRANSPOSITION OF THE GREAT VESSELS: A FIVE-YEAR SURVEY

Thomas G. Baffes, M.D., Maurice Lev, M.D. (by invitation), Milton H. Paul, M.D. (by invitation), Robert A. Miller, M.D. (by invitation), William L. Riker, M.D. (by invitation), Arthur De Boer, M.D. (by invitation), and Willis J. Potts, M.D., Chicago, Ill.

THE PROBLEM of surgical treatment of transposition of the great vessels still remains unsolved. It is not a simple matter of establishing serial continuity of the pulmonary and systemic circulations. True, the technical difficulties of such procedures are better understood, and successful complete correction of transposition has been reported.[1] However, the problem extends far beyond surgical technique. The pulmonary artery in cases of transposition comes off the left ventricle and the lungs are usually subjected to high arterial pressure. The consequences of this anatomic relationship are not completely understood, but it is expected that prolonged high pulmonary arterial pressure is harmful. Correction of transposition of the great vessels is also complicated by the relationship of any potential surgical procedure to growth. Patients with transposition defects become critically ill and require surgical correction very early in life. Suture lines or artificial prostheses used for early surgical palliation may impede flow of blood by the time the infant reaches adulthood. The matter of timing is extremely important, and it remains to be seen whether total correction or staged partial correction will give the best ultimate physiologic results. Finally, the pathologic condition of transposition of the great vessels is not uniform. A variety of associated defects may be encountered. It is highly probable that no single operative procedure will be applicable to all of them. The final answer to the transposition defect still eludes us. It is our hope only that the material in this paper might help crystallize some thoughts on the subject and lead to more steps in the right direction. It is also an opportunity to describe our results in a palliative procedure which has provided very satisfactory clinical results to date.

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MATERIAL

The first patient operated upon by us for transposition of the great vessels by the method of transplanting the inferior vena cava and the right pulmonary veins was reported from the Children's Memorial Hospital in Chicago. The operation was performed in March, 1955. Five years have elapsed since that time and 148 similar procedures have been done. The age of these patients at the time of operation has varied from 6 days to 15 years. We have analyzed the first 117 operative procedures for mortality rate, clinical results, and 6-month to 5-year postoperative follow-up. The remaining 31 patients have been separated into a second group because of a shorter postoperative follow-up and because Teflon grafts were used for the procedure. The pathology of transposition of the great vessels has been re-evaluated in the light of our operative experience. Catheterization data and other physiologic studies were collected, wherever feasible, and are described as a guide to clinical selection of patients for this procedure.

PARTIAL CORRECTION OF TRANSPOSITION OF THE GREAT VESSELS

The basic steps for transfer of the inferior vena cava and the right pulmonary veins have not been altered (Fig. 1). As described in our earlier articles,[2, 3] a thoracotomy is done through the right fifth interspace and the right pulmonary artery is dissected free. A major change from the original description, however, involves early occlusion of the right main pulmonary artery, immediately after the thoracotomy incision is completed. This alteration in technique is important. It has reduced the operative mortality from about 50 per cent to its present rate of about 10 per cent. As is well known, pulmonary arterial pressure is high in most cases of transposition. The manipulation of the lung required for operation can often lead to such serious pulmonary hemorrhage that the patient dies in the immediate postoperative period from marked hemorrhagic pulmonary congestion. Early occlusion of the pulmonary artery, before dissection of the other hilar structures, will generally avoid this complication.

After the right main pulmonary artery is occluded, the right pulmonary veins, the lateral aspect of the right atrium, the right phrenic nerve, the inferior vena cava, and the right main-stem bronchus are dissected free. The pericardium is utilized to suspend the heart from the chest wall, so that the weight of the enlarged heart does not cause collapse of the left lung. This is another important change in technique. It has made possible survival of a number of tiny infants who would certainly have died of anoxia during the procedure. Hypothermia is also used to advantage. We have found that reduction of the patient's body temperature to about 30° C. occasionally permits survival of an infant who will not tolerate occlusion of the pulmonary artery at normal body temperature.

After adequate cooling of the patient, temporary occlusion of the right main pulmonary artery, suspension of the heart with the pericardium, and isolation of the remaining hilar structures, the following maneuvers are completed. (1) A curved coarctation clamp is placed on the lateral aspect of the inferior vena cava and a homologous aortic graft is anastomosed to the excluded lip of the inferior vena cava (Fig. 1, *B* and *C*). (2) The right pulmonary veins are separated from their point of entrance into the left atrium and the opposite end of the aortic homograft is anastomosed to the left atrial stump of the right pulmonary veins (Fig. 1, *D*, *E*, and *F*). (3) A curved coarctation clamp is then applied to the lateral aspect of the right atrium and the distal end of the right pulmonary veins is anastomosed to the excluded lip of the right atrium (Fig. 1, *F* and *G*). (4) The occluding umbilican tape ligatures about the right main pulmonary artery and the right main-stem bronchus are then removed and the right lung is allowed to expand. (5) The patient is given a few moments to recover, and a stout silk ligature is tied about the point of entrance of the inferior vena cava into the right atrium. This makes the flow of blood from the inferior vena cava, through the aortic homograft into the left

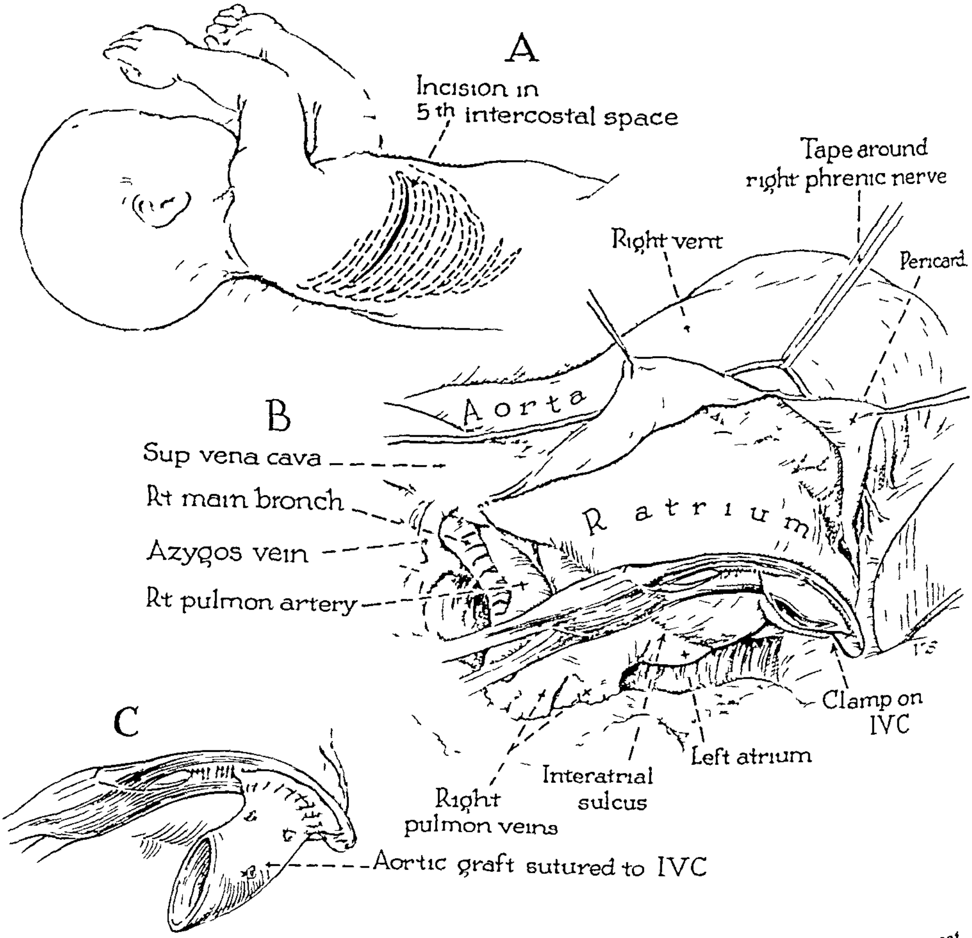


Fig 1.—Diagram of operative procedure for partial correction of transposition of the great vessels by transferring the inferior vena cava and the right pulmonary veins (see text)

atrium, obligatory. (6) The pericardial incision is then repaired, endothoracic drainage is provided, and the thoracotomy is closed.

One hundred and seventeen patients have undergone the procedure just described, with homologous aortic grafts used to bypass the inferior vena cava. The mortality rate has improved steadily. Early in the series, it was 50 per cent. During the last year, however, it decreased to 8.3 per cent. The over-all operative mortality, including immediate and delayed operative deaths, was 29.0 per cent (Table I). In the latter half of the past five years, the operative mortality has also greatly improved for the younger patients in the series (Table II). Early in our efforts, most of the younger patients were between 4 and 6 months of age, hence the residual high mortality shown for that age group. As more experience accumulated, however, patients below 3 months of age were operated upon and the mortality rate in those infants is comparable

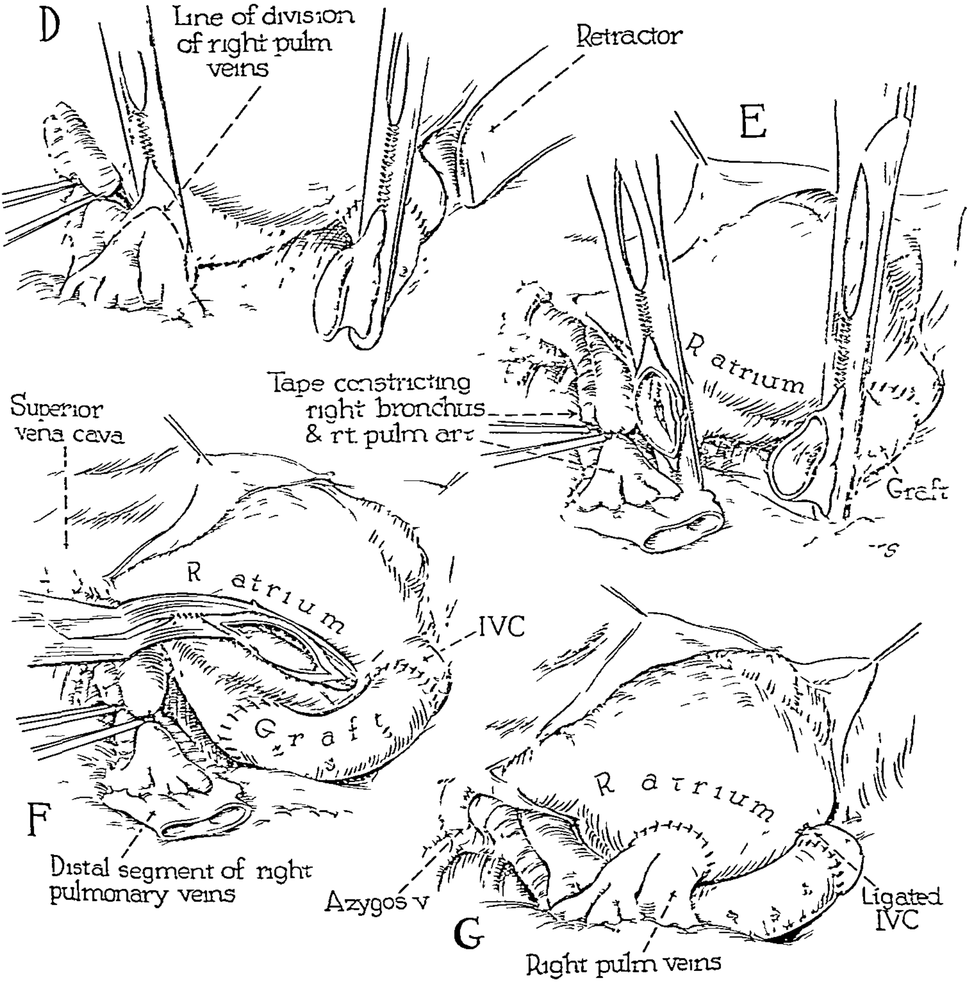

D
Line of division of right pulm veins
Retractor
E
R atrium
Tape constricting right bronchus & rt. pulm art
Graft
Superior vena cava
R atrium
IVC
Graft
F
Distal segment of right pulmonary veins
R atrium
Azygos v
G
Right pulm veins
Ligated IVC

Fig 1.—Cont'd. *For legend see opposite page*

to the over-all mortality. At the present time, any child with a transposition defect who is deemed a satisfactory operative risk is operated upon regardless of age.

TABLE I.

YEARS	TOTAL NO. OF CASES	OPERATIVE DEATHS	MORTALITY RATE (%)
1955-56	36	18	50.0
1957	22	10	45.5
1958	35	4	11.4
1959	24	2	8.3
Totals	117	34	29.0

TABLE II.

AGE	TOTAL NO. OF CASES	OPERATIVE DEATHS	MORTALITY RATE (%)
0-3 mo.	13	4	30.8
4-6 mo.	10	6	60.0
7 mo.-1 yr.	20	5	25.0
2-5 yr.	47	12	25.5
Over 5 yr.	27	7	25.9
Totals	117	34	29.0

Postoperative results have been very satisfactory. Eighty-three patients in the above series survived operation and have had 6 months to 5 years of postoperative observation (Table III). Fifty-eight patients (70 per cent) had minimal residual cyanosis following partial correction of their transposition defect. Their exercise tolerance was markedly improved, and weight and muscular development approached normal limits, even in the youngest members of the group. Episodes of severe dyspnea and cardiac failure became rare. Ultimately, they were able to discontinue taking digitalis and diuretics. Roentgenograms, in most instances, showed decrease in the size of the heart shadow (Fig. 2).

TABLE III.

	CASES	PER CENT
Good results	58	70.0
Fair results	18	21.6
Poor results	2	2.4
Lost to follow-up	5	6.0
Totals	83	100.0

Eighteen patients (21.6 per cent) had mild cyanosis at rest which increased considerably on exercise. Their clinical results were classified as fair. Although episodes of dyspnea and heart failure had decreased, they continued to have significant impairment in exercise tolerance. Muscular development, although greatly improved, was considered below normal. Roentgenograms usually demonstrated no decrease in heart size. Two patients (2.4 per cent) had poor clinical results. Their cyanosis did not improve at all after operation, and they both ultimately succumbed, although they did not die until several months following operation. Five patients who survived operation (6.0 per cent) were lost to long-range follow-up.

Causes of operative death are recorded in Table IV. Thirty patients died in the hospital immediately following operation. Thirteen developed intractable cardiac failure and 3 had cerebral vascular accidents from which they did not recover. These deaths were considered hazards of the transposition defect and in a sense are not preventable. Six patients, however, died of severe pulmonary hemorrhage during or immediately following operation, and 5 infants succumbed to severe edema of the right lung which caused fatal anoxia in the immediate postoperative period. We felt that these deaths were preventable because they presumably resulted from incomplete management of the high pressure in the pulmonary artery. Since early occlusion of the right main pulmonary artery has been incorporated into the operative procedure, such deaths have virtually disappeared. The remaining immediate operative deaths, 2 from intercostal hemorrhage and 1 from supraventricular tachycardia, are technical hazards and probably can be prevented by meticulous attention to surgical and medical management.

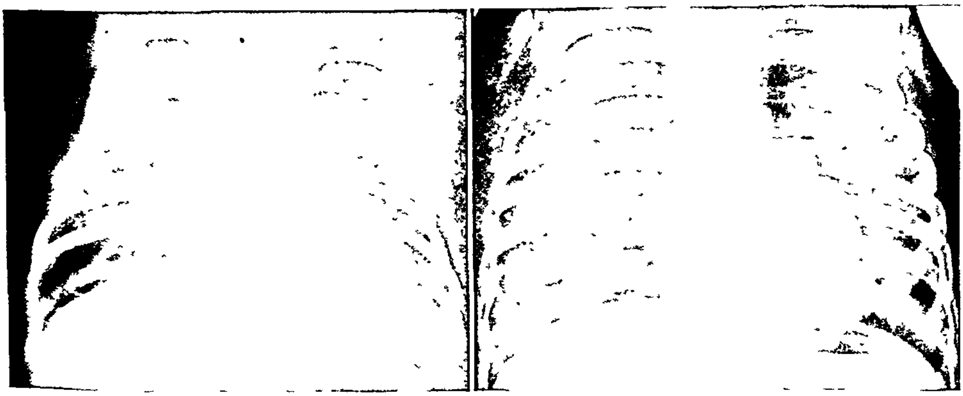

A. B.

Fig. 2.—Roentgenograms of the chest which demonstrate decrease in size of the heart shadow following partial correction of the transposition defect. *A*, Preoperative chest roentgenogram. Note marked cardiac enlargement. *B*, postoperative chest roentgenogram taken about 3 years after surgery. The cardiac shadow has greatly decreased in size.

TABLE IV. CAUSES OF DEATH

Immediate Operative Deaths	
1. Cardiac failure	13
2. Cerebral vascular accidents	3
3. Hemorrhage from right lung	6
4. Right pulmonary edema with anoxia	5
5. Intercostal hemorrhage	2
6. Supraventricular tachycardia	1
Delayed Operative Deaths	
1. Diarrhea	1
2. Pulmonary arteriolar sclerosis	3

Four patients died shortly after returning to their homes. One contracted severe infantile diarrhea and succumbed to dehydration. It is felt that this death is not directly related to the operative procedure. Three patients, however, did not have satisfactory response to the operative procedure. They were still very cyanotic when discharged after prolonged hospitalization, and died suddenly and unexpectedly with terminal syndromes variously interpreted as "pneumonitis" or "pulmonary congestion." Although their postmortem examinations were not performed at our hospital, all three autopsies were reported as showing pulmonary arteriolar sclerosis.

Clinical results and operative deaths were studied in order to establish indications for this surgical procedure. It was noted that only fair clinical results were obtained in patients having high preoperative arterial oxygen saturations, while best results were obtained in children with intense cyanosis. Hence, we no longer operate upon patients with transposition defects with arterial oxygen saturations of 75 per cent or over. Such moderately cyanotic patients with transposition have good shunts across the septal defects, or other intracardiac deformities which permit mixing of the pulmonary and systemic circulations. This type of surgical procedure does not result in significant improvement of the peripheral arterial saturation.

Another important consideration is the presence of high pulmonary arterial pressure. Its role in the postoperative course of patients with transposition defects has been extremely difficult to evaluate. At this time, its presence does not influence our choice of patients for this operation.

Moderate pulmonary valvular or infundibular stenosis has not impaired our clinical results. In fact, some of the most striking instances of postoperative improvement in cyanosis have occurred in patients with mild pulmonary stenosis. Our conviction that pulmonary stenosis should not be a contraindication to this procedure is strengthened by evaluation of 14 patients with pulmonary artery pressures below 200 mm. of water who were treated with aorticopulmonary or subclavian-pulmonary anastomoses (Table V). The immediate postoperative mortality rate for these operative procedures was 50 per cent, and improvement in cyanosis was not as satisfactory as in similar patients having transfer of the inferior vena cava and the right pulmonary veins. Long range follow-up reveals that only 1 of the 7 survivors is still alive. He has recently had to return to the hospital for a second shunt operation.

TABLE V.

SHUNTS	TOTAL NO. OF CASES	OPERATIVE DEATHS	MORTALITY RATE (%)
Aorticopulmonary	6	5	83.4
Subclavian-pulmonary	8	2	25.0
Totals	14	7	50.0

Cardiac failure is a common finding in transposition of the great vessels. We have never considered it a contraindication to operation, if the patient responds to medical treatment. Approximately one half the patients operated upon were in severe failure when they arrived at the hospital, yet after adequate preparation many of these survived the operative procedure and have had excellent clinical results. The only patients denied operation were those who remained in intractable heart failure in spite of intensive and prolonged medical therapy.

PHYSIOLOGIC OBSERVATIONS

Transposition of the great vessels can usually be differentiated from other forms of cyanotic congenital heart disease on the basis of clinical, roentgenographic, and electrocardiographic examination. Whenever these findings are classical it is usually possible to select a suitable surgical candidate on the basis of the presence of intense cyanosis. Nevertheless, selective or venous angiocardiography is frequently performed and is of particular value in demonstrating the presence of associated intracardiac lesions.

Data obtained at right heart catheterization may also assist in selection of surgical candidates. Table VI presents the pre- and postoperative peripheral arterial oxygen saturations of 6 patients ranging in age from 7 weeks to 8 years at the time of surgery. The postoperative arterial saturations in this group were 78 to 84 per cent at rest, and this latter figure is considered to be the approximate maximal obtainable saturation. The marked increase in arterial oxygen saturation from approximately 40 per cent (preoperatively) to 80 per cent (postoperatively) in patients J. L. and R. H. was associated with dramatic clinical improvement (Figs. 3 and 4). These patients had considerably elevated pulmonary arterial pressures in the preoperative studies. However, pulmonary vascular resistance was not significantly increased in the face of large pulmonary blood flow (Table VI). Large left-to-right atrial shunts resulted from the surgical transposition of the right pulmonary veins from the left to the atrium.

TABLE VI.

PATIENT	AGE	PULMONARY ARTERY PRESSURE (MM. Hg)	PULM./SYST. BLOOD FLOW* (L./MIN./M².)	SYST. ARTERIAL (%) (PREOP.)	O₂ SATURATIONS (%) (POSTOP.)
J. L.	4 wk.	62/27 (47)†	12.2/5.2	42	78
R. H.	8 mo.	62/30 (50)	12.1/5.3	39	84
S. G.	4 wk.	— —	—	69	81
D. M.	3 yr.	38/15 (25)	6.4/3.4	66	84
S. M.	8 yr.	27/10 (17)	—	57	79
M. B.	8 yr.	100/72 (86)	7.2/4.5	77	81

*Oxygen consumption estimated at 170 ml./min./M.² with all studies performed under Demerol-Sparine-Phenergan premedication.

†Mean arterial pressures.

Patients D. M. and S. M. had proportionately less increase in arterial oxygen saturation following surgery, but each reached a level of approximately 80 per cent and had marked clinical improvement (Table VI). It is apparent that moderate stenosis of the left ventricular outflow tract is not a contraindication to the partial venous correction procedure. Patients D. M. and S. M. had clinical and catheterization evidence of pulmonary stenosis with moderately low pulmonary artery pressure but increased pulmonary blood flow. Of considerable interest in this regard is the added observation in patient J. L. (Fig. 3) that left ventricular outflow tract stenosis developed in the 5-month interval between the preoperative and postoperative catheterization studies.

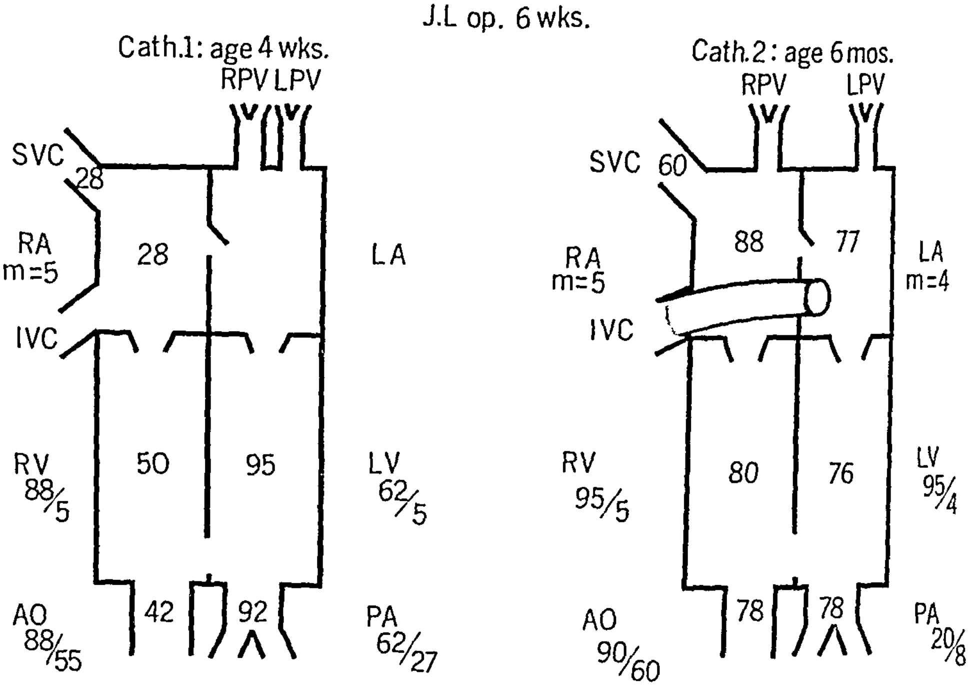


Fig. 3.—Preoperative and postoperative catheterization data on patient J. L. He was catheterized at the age of 4 weeks *(left diagram)* and operated upon at 6 weeks of age. Postoperative catheterization was done at 6 months of age *(right diagram)*. Note apparent development of stenosis of left ventricular outflow tract in the postoperative period (see text).

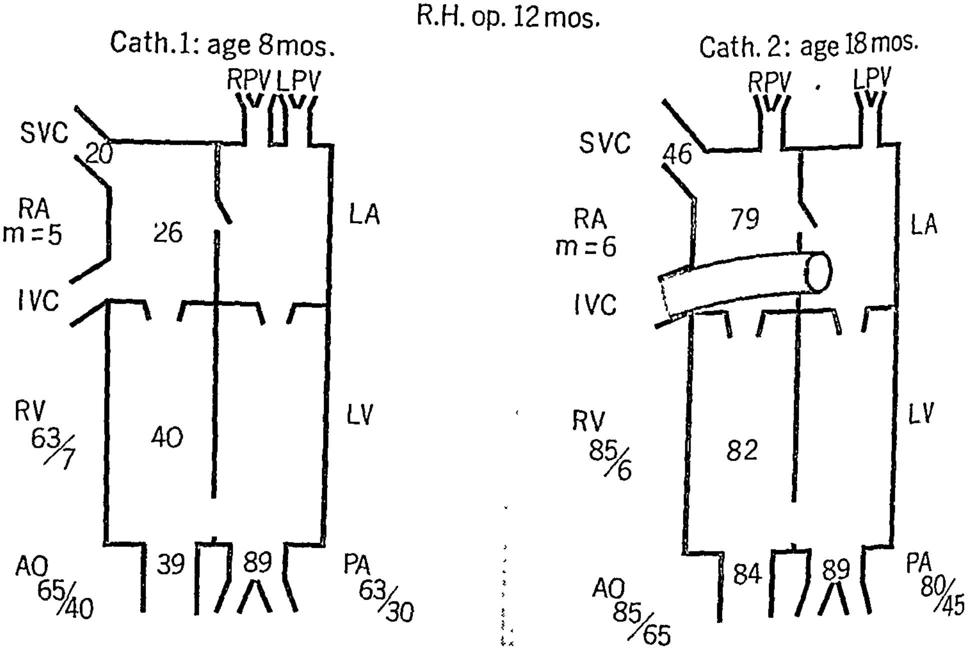


Fig. 4.—Preoperative and postoperative catheterization data on patient R. H. He was catheterized at the age of 8 months *(left diagram)* and operated upon at 12 months of age. Postoperative catheterization was done at the age of 18 months *(right diagram)*.

Partial venous correction has been performed on a few children with markedly increased pulmonary vascular resistance but, as previously stated, there has been only minimal or moderate clinical improvement in this group. M. B. represents such a patient (Table VI), with a preoperative arterial oxygen saturation of 77 per cent and a moderately large left-to-right shunt at the ventricular level associated with severe pulmonary vascular obstruction. The postoperative increase in arterial saturation to 81 per cent was associated with slight clinical improvement

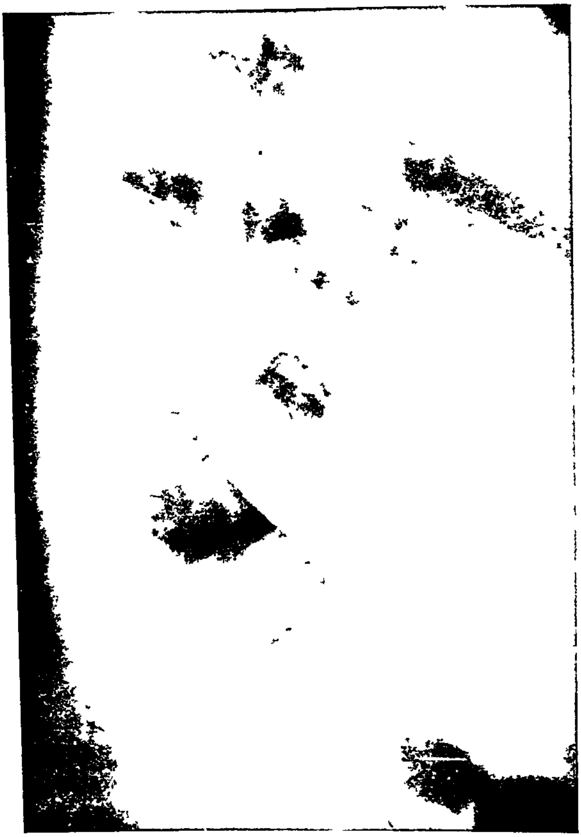
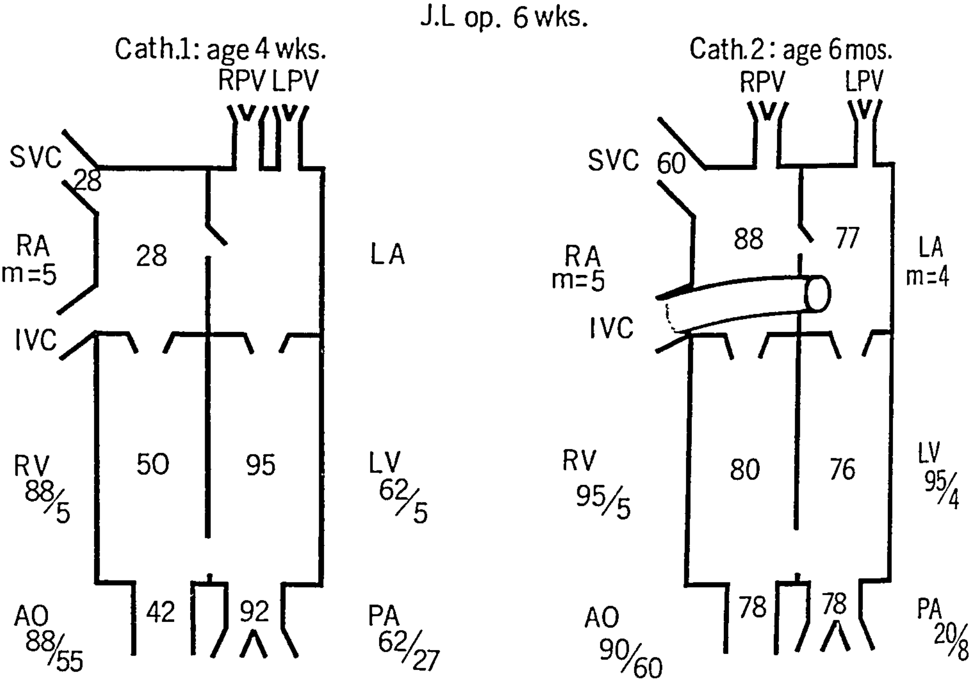


Fig 5 —Postoperative venous angiogram through inferior vena cava which demonstrates large thrombus formation at upper end of a Teflon prosthesis used to transfer the inferior vena cava to the left atrium

USE OF TEFLON PROSTHESIS

Since September, 1959, when the series reported in the earlier section of this paper was completed, use of homologous aortic grafts has been discontinued and Teflon prostheses have been inserted to transfer the inferior vena from the right atrium to the left atrium. Otherwise the operative procedure is the same as that just described Thirty-one patients have now been operated upon with the use of Teflon prostheses. Eleven of these patients have died following operation, an immediate operative mortality rate of 35 5 per cent. In general, the



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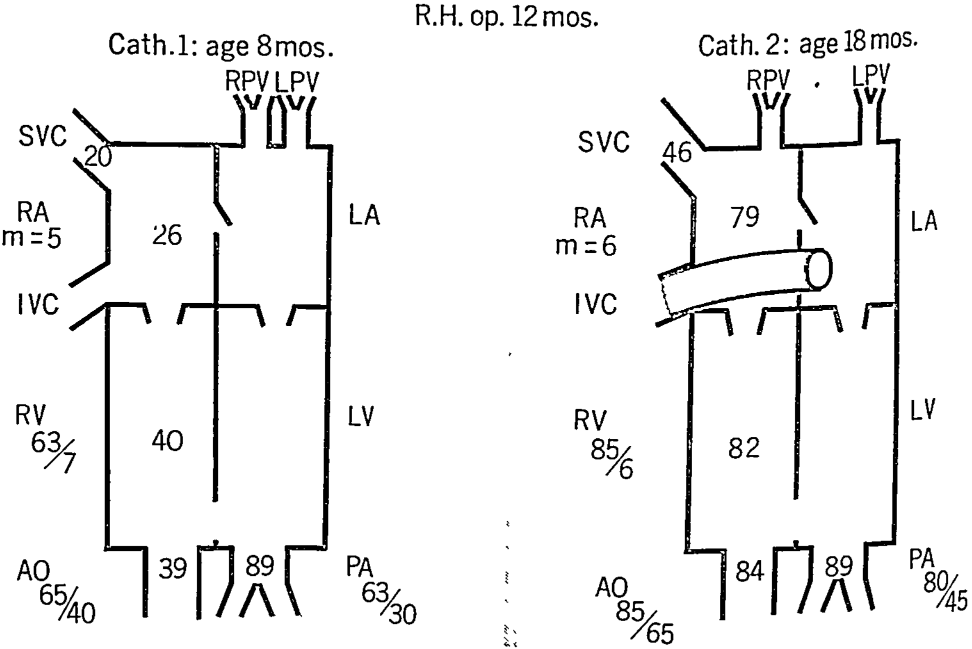

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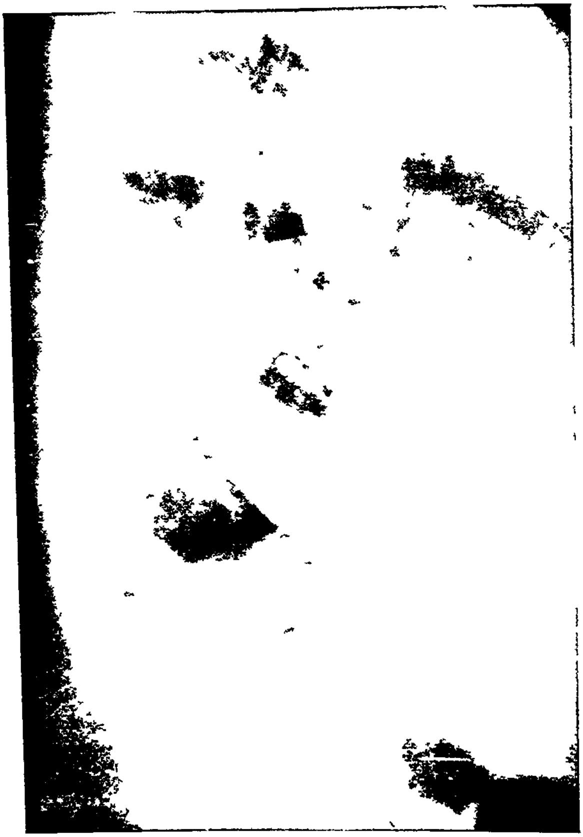

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This one definite instance of thrombus formation in the Teflon prosthesis is in keeping with our own observations in the laboratory that there is a slightly higher incidence of thrombus formation with plastic prostheses than with homologous aortic grafts. However, it is true, as in other types of cardiovascular operations, that plastic prostheses have greatly facilitated introduction of artificial conduits. The incidence of thrombus formation is relatively small and should decrease with further experience. It has not occurred since the single episode early in the series. We do not have long-term follow-up studies of replacement of the inferior vena cava by Teflon prostheses in human beings. However, these have been introduced into animals which have been followed thus far for 16 months without serious complications. We feel that Teflon prostheses can be used to replace homologous aortic grafts in this operative procedure.

SUMMARY

1. Five years' experience with partial correction of transposition of the great vessels by transplanting the inferior vena cava and the right pulmonary veins is described.

2. One hundred and forty-eight patients have been operated upon in this manner; homologous aortic grafts were used in 117 instances and Teflon prostheses were used in 31.

3. The operative procedures with homologous aortic grafts were analyzed with regard to mortality rate, long-range clinical results, causes of death, and available physiologic data.

4. Our opinions and methods for proper selection of patients for this operative procedure are discussed.

REFERENCES

1. Senning, A.: Surgical Correction of Transposition of the Great Vessels, Surgery 45: 966, 1959.
2. Baffes, T. G.: A New Method for Surgical Correction of Transposition of the Aorta and Pulmonary Artery, Surg. Gynec. & Obst. 102: 227, 1956.
3. Baffes, T. G., Riker, W. L., De Boer, A., and Potts, W. J.: Surgical Correction of Transposition of Aorta and Pulmonary Artery, J. THORACIC SURG. 34: 469, 1957.

DISCUSSION

DR. DENTON A. COOLEY, Houston, Texas.—Anyone familiar with the physiologic, anatomic, and technical problems concerned with surgical correction of complete transposition of the great vessels must admire the results which Dr. Baffes has reported. The operation which he is using is, of course, palliative in nature and not a complete repair. We have used this technique in 4 patients with fair or good results. One drawback, in my opinion, is that the operation is complicated and technically difficult, particularly in small infants.

Our preference for most cyanotic transpositions is for the Blalock-Hanlon operation of creation of an interatrial septal defect. This procedure is well tolerated by infants since the technique is simple and may be accomplished quickly. It avoids using a graft in the venous system which may be too small as the infant grows and is subject to the well-known thrombotic complications of grafts placed in the veins. The Blalock-Hanlon procedure does not eliminate the possibility of future total correction of the anomaly when a satisfactory technique is ultimately developed.

(Slide) We have used the Blalock-Hanlon technique in 62 patients, most of whom were small infants, often in extremis from severe cyanosis. In the last 31 patients there were three deaths and results in the survivors were considered good or satisfactory in most. Unfortunately it is difficult to be completely objective in evaluating the results, but survival itself is a favorable recommendation of the procedure.

Finally, however, I would like to compliment Dr. Baffes on his outstanding contribution in treatment of this challenging lesion.

DR. BAFFES (Closing).—Dr. Senning's total correction procedure has a great deal of merit, because it is relatively simple. It can be done in about 18 minutes, which is a remarkable thing.

It has also another advantage, in that it has incomplete suture lines, which probably will provide for growth. We have talked this out many times, and it seems to us that three things must be done for the *transposition complexes*:

1. Some kind of technical method must be developed to put the systemic and pulmonic circulations in series. Senning's technique is an excellent one. Perhaps an arterial method will be developed in the future.

2. The patient must be allowed to grow. We shouldn't overlook that factor.

3. The pulmonary hypertension must be accounted for and taken care of. It seems to me that possibly some type of banding procedure in combination with the Blalock-Hanlon might be a preliminary method in infant transpositions.

I'd like to show you one method of total correction that we are thinking about. This method is a venous correction and tries to encompass all the factors just mentioned.

(Slide) We have found that in total corrections there are two difficulties. Either both circulations are asked to cross an atrial septal defect which is almost impossible for them to do, or the atrial chambers are distorted in such a way that they impede the drainage of the pulmonary veins. The patients die of anoxia or edema a few hours after the operation, although they get through the operation fairly well.

In this procedure, the inferior vena cava is sutured directly to the left atrium while the pulmonary circulation is shunted through an atrial defect with an Ivalon patch. The superior vena cava is shunted directly through the right main pulmonary artery. I don't know whether it's going to work or not. We haven't had the opportunity to try it yet.

SURGICAL PALLIATION IN PATIENTS WITH EBSTEIN'S ANOMALY AND CONGENITAL HYPOPLASIA OF THE RIGHT VENTRICLE

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Ebstein's anomaly is an uncommon congenital malformation of the heart, presumably caused by an arrest in the development and positioning of the tricuspid valve. The valve leaflets are attached near the midportion of the right ventricle, reducing the capacity of the ventricle to a varying degree. The excluded segment of right ventricle usually takes on the thin-walled and distensible characteristics of the adjacent right atrium. The resulting small ventricular chamber is, in effect, an area of resistance to right atrial emptying, reflected in the atrium by distention, hypertrophy, and elevation of pressure. These responses, basic to Ebstein's anomaly, are identical to those of the very rare isolated hypoplasia of the right ventricle. There is an interatrial communication in approximately one half of the cases of Ebstein's anomaly, either a patent foramen ovale or an atrial septal defect, through which right-to-left shunting of blood may take place. The displaced tricuspid valve may function normally or may be incompetent. In the occasional patient with minimal reduction of right ventricular volume, no symptoms are present and the patient may have a normal life expectancy. In most cases, however, symptoms are present in childhood, or even in infancy, and are progressive. The majority of the patients will eventually become cyanotic, because of right-to-left shunting at the atrial level or chronic congestive heart failure, and death usually occurs in the first or second decade of life.

During the past year we reported a case of congenital hypoplasia of the right ventricle with an associated atrial septal defect in which a superior vena cava–distal right main pulmonary artery (SVC-RPA) anastomosis was

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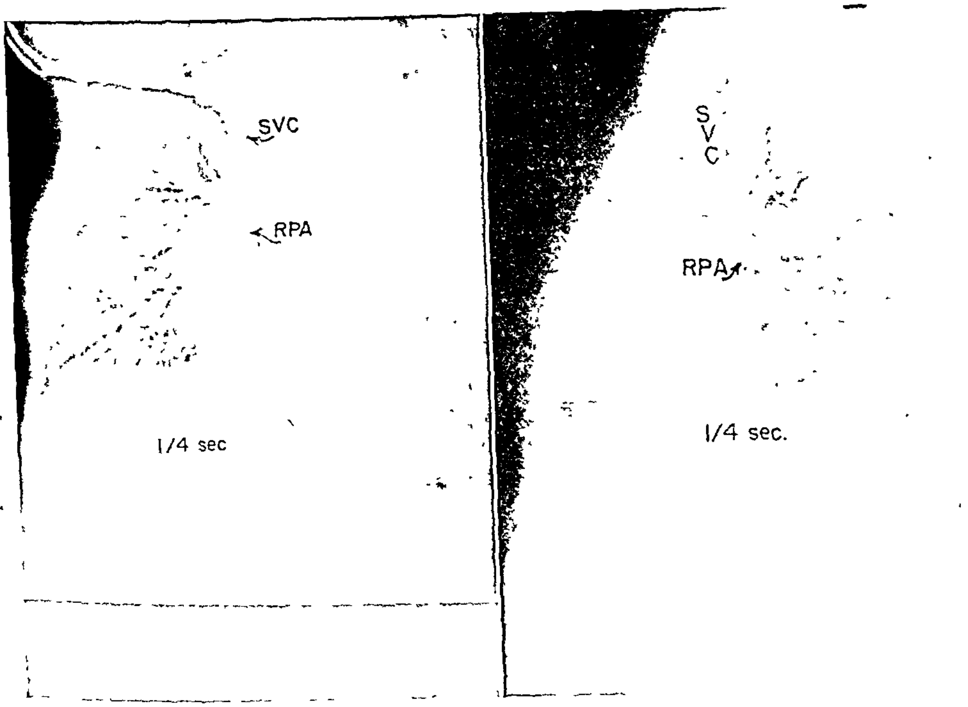
performed.[1] This procedure, which had been suggested several years ago by Glenn[2, 3] for palliation in Ebstein's anomaly, reduces blood flow to the right atrium by approximately 35 per cent, and thereby seemed to be ideally suited to relieve the right atrial distention and pressure elevation. Similar anastomoses have been performed in 3 patients with Ebstein's anomaly, 2 of whom were briefly mentioned in an addendum to the initial report.[1]



A.

B.

Fig. 1.—Case 1. *A* and *B*, Angiocardiograms which demonstrate flow of opaque medium from superior vena cava directly into right main pulmonary artery through end-to-end anastomosis.

CASE REPORTS

Case 1.—A 4-year-old cyanotic child was admitted to the Cook County Hospital on March 26, 1959, with a history of a previous admission at the age of 2 in congestive heart failure. The child was small and thin, dyspnea and fatigue were noted on exercise, and clubbing of the nail beds was present. The clinical and accessory laboratory findings, including angiocardiography and cardiac catheterization, demonstrated enlargement and hypertrophy of the right atrium, a mean right atrial pressure of 7 mm. Hg, and a mixed shunt at the atrial level, predominantly right-to-left. The peripheral arterial oxygen saturation was 80.6 per cent of capacity. A diagnosis of Ebstein's anomaly was considered, but no displacement of the tricuspid valve could be demonstrated.

An exploratory operation was performed on June 19, 1959, with a probable diagnosis of tricuspid stenosis. The operative findings confirmed the presence of an atrial septal defect, and, combined with the preoperative data, suggested a diagnosis of hypoplasia of the right ventricle. The performance of a SVC-RPA anastomosis was considered at this time, but the sternal splitting incision, in the opinion of the surgeon, did *not* permit adequate access to the vessels. The child was allowed to recover from the operation, and on July 17, 1959, was re explored through a right anterolateral incision in the fourth intercostal space. An end to end SVC-RPA anastomosis was performed without difficulty, during a 12-minute period of superior vena caval occlusion (Fig. 1). At the operating table, a marked decrease in right atrial distention was observed, and pressures recorded in the right atrium fell from a preshunt mean level of 8 mm. Hg to 0 after completion of the anastomosis (Fig. 2). The atrial septal defect was not closed, since it was thought that an additional site of decompression might be desirable with growth of the child. Recovery was uneventful, and, on discharge clinical findings were compatible with a reduction of right atrial pressure.

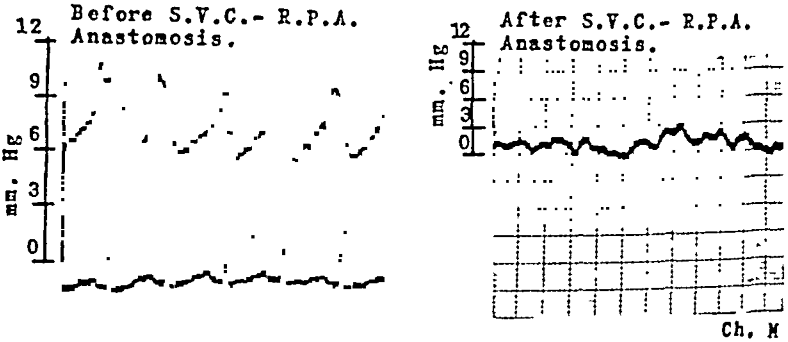


Fig. 2.—Case 1. Right atrial pressures recorded during surgery, with chest open, before and after SVC-RPA anastomosis.

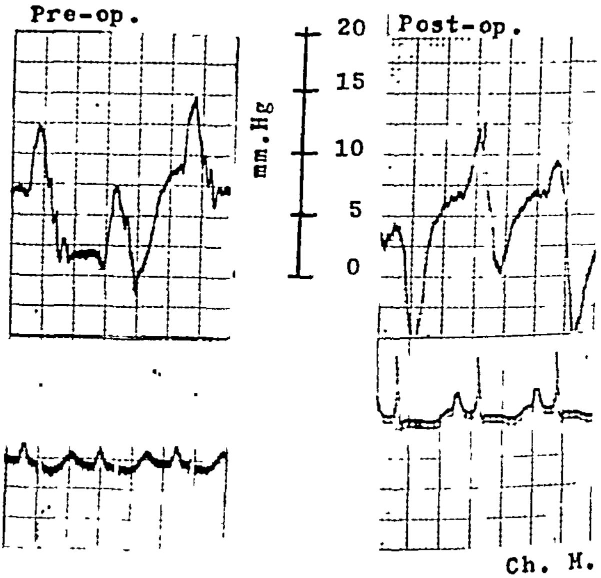
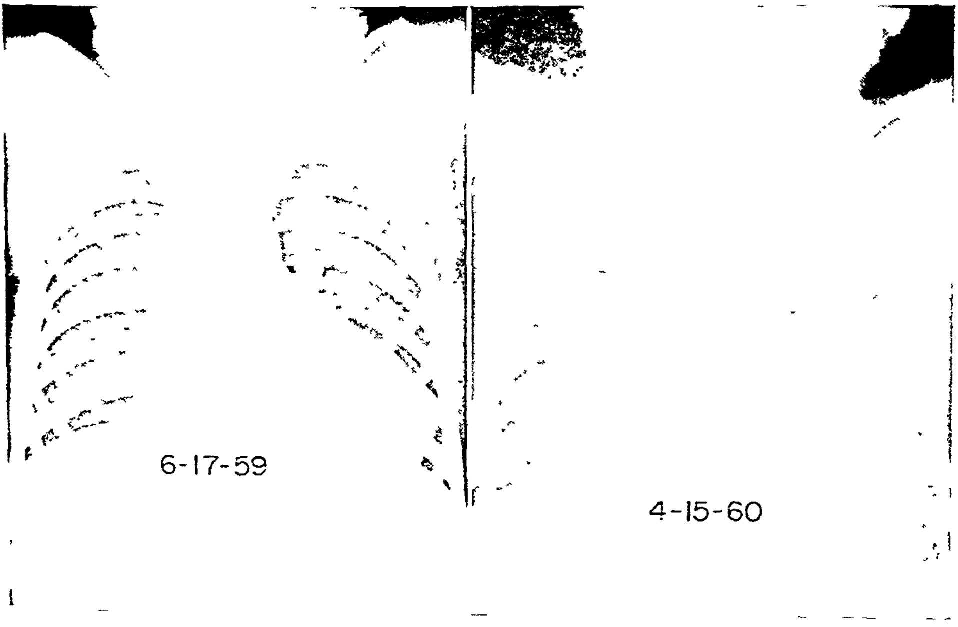


Fig. 3.—Case 1. Right atrial pressures recorded at cardiac catheterization before and 2 months after SVC-RPA anastomosis.

The child was readmitted 3 months after operation for repeat studies. Symptomatic improvement was evident, with increasing exercise tolerance, a definite gain in physical and mental development, and disappearance of the cyanosis. Heart size, however, was similar to that of the preoperative size as shown on x-ray studies of the chest, and the electrocardiogram demonstrated similar evidences of right atrial hypertrophy. On cardiac catheterization, the mean right atrial pressure was 4 mm. Hg, the peripheral arterial oxygen saturation was 89.4 per cent of capacity, and a clearly predominant left-to-right shunt at the atrial level was demonstrated (Fig. 3 and Table I).

TABLE I. CASE 1. PERTINENT PHYSIOLOGIC DATA, BEFORE AND AFTER SVC-RPA ANASTOMOSIS

	PREOPERATIVE	POSTOPERATIVE (2 MONTHS)
Right atrial pressure (mean)	7 mm. Hg	4 mm. Hg
Peripheral arterial O_2 saturation	80.6%	89.4%
Pulmonary blood flow	4.25 L./min./M.^{2}	6.77 L./min./M.^{2}
Systemic blood flow	5.02 L./min./M.^{2}	4.35 L./min./M.^{2}



A. *B.*

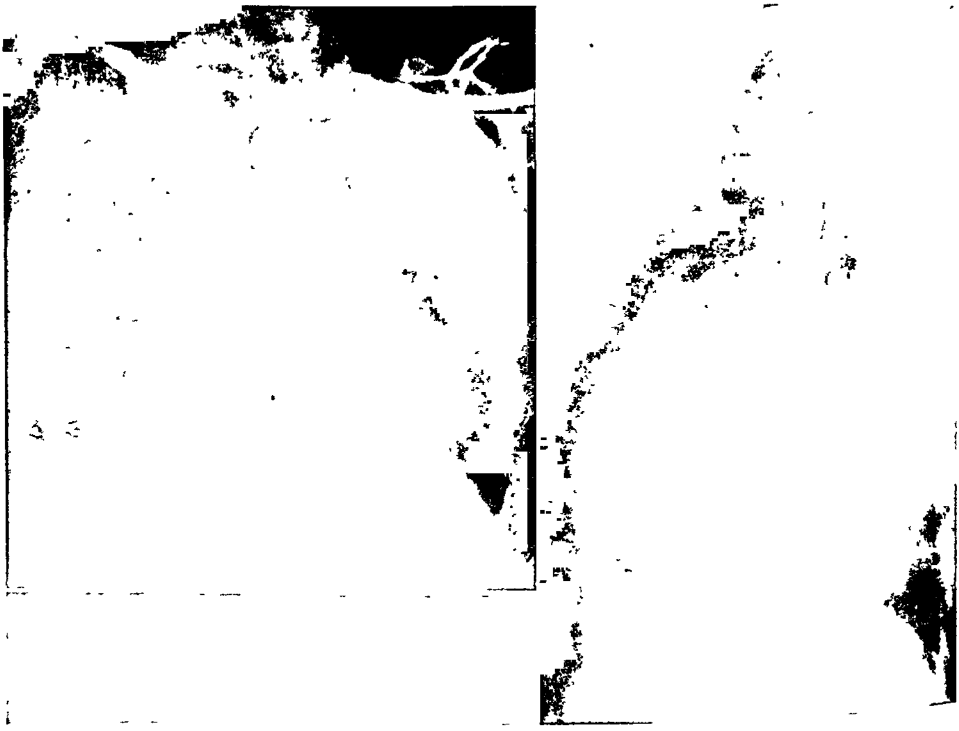
FIG. 4.—Case 1. *A* and *B*, Roentgenograms of the chest taken before and 9 months after SVC-RPA anastomosis. Film of April 15, 1960, was taken with child in congestive heart failure.

Approximately 9 months after operation, she was again admitted to the hospital, showing signs of congestive heart failure with cardiac enlargement evident on x-ray studies. Cardiac enlargement has persisted (Fig. 4), even though she responded promptly to digitalization with disappearance of the other signs of congestive heart failure. At the present time, symptomatic and developmental improvement over her preoperative status is still evident, and she remains acyanotic. Closure of the atrial septal defect in this child is being considered.

CASE 2.—A 14-year-old child was admitted to the Presbyterian-St. Luke's Hospital on July 26, 1959, with a history of progressive dyspnea and cyanosis on minimal exertion. The child appeared chronically ill, physical activity was markedly limited, the heart was massively enlarged, and the pulse was grossly irregular. The physical and laboratory findings were diagnostic of Ebstein's anomaly. Cardiac catheterization performed in 1956 showed a mean right atrial pressure of 16 mm. Hg and demonstrated the displacement of the tricuspid valve.

An end-to-end SVC-RPA anastomosis was performed on July 29, 1959, which required 12 minutes of superior vena caval occlusion. A significant lowering of right atrial pressure was recorded following completion of the anastomosis. Immediately after operation, petechiae were noted over the face and neck. Within another 12 hours the child was disoriented and the rectal temperature was 105.2 F. The fever was controlled with hypothermia blankets for 48 hours, after which the temperature stabilized near normal levels and the disorientation cleared. On the fourth postoperative day, however, the child died following a rapidly progressive episode of dyspnea, cyanosis, and vascular collapse.

An autopsy demonstrated the characteristic displacement of the tricuspid valve, a patent foramen ovale, and a thrombus in the proximal stump of the right main pulmonary artery, propagating to occlude the left main pulmonary artery.



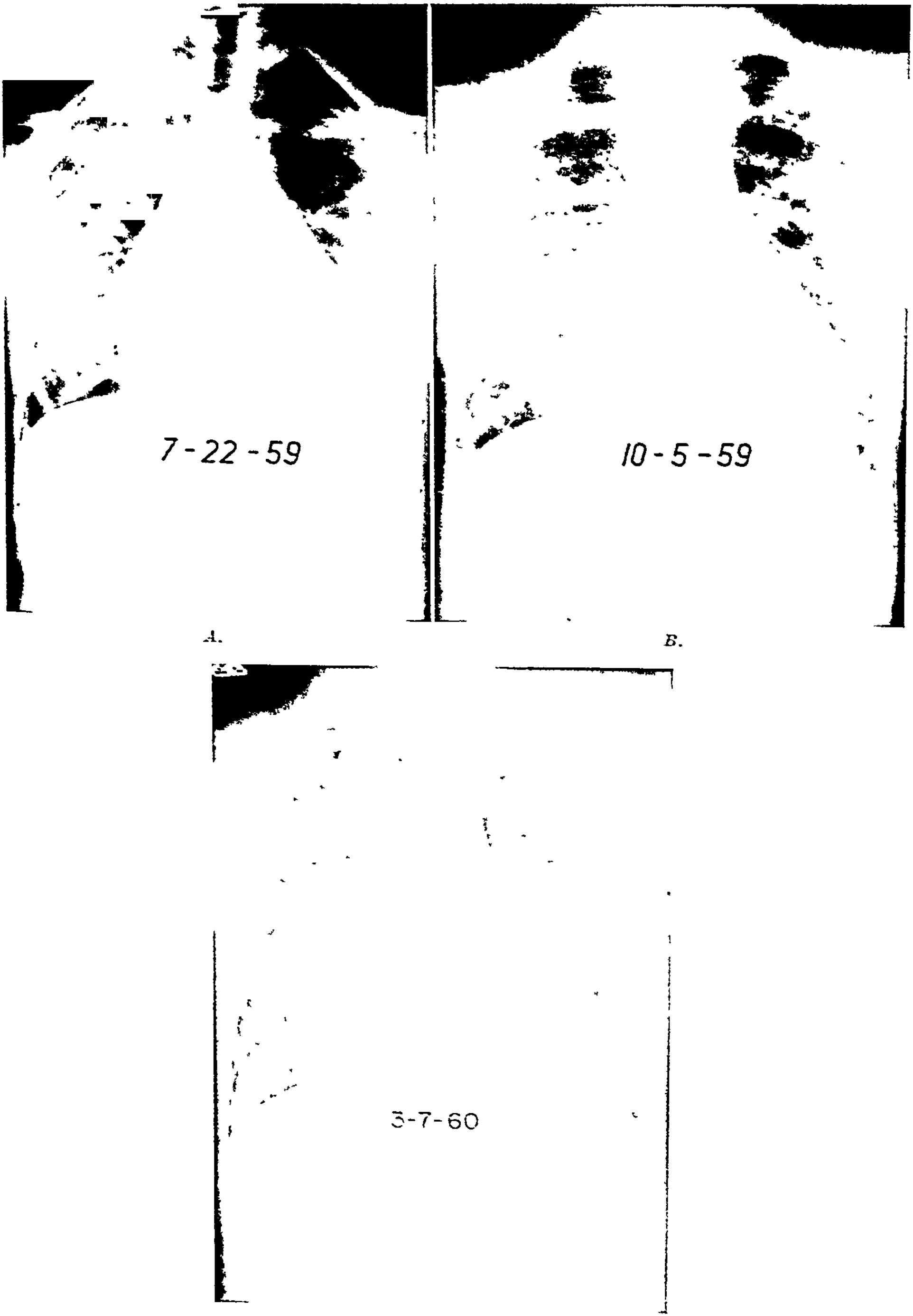
A. *B.*

Fig. 5.—Case 3. *A* and *B*, Angiocardiograms which demonstrate flow of opaque medium through side-to-end SVC-RPA anastomosis. The right pulmonary veins and the left atrium are also faintly opacified.

Case 3.—An 8-year-old child with a diagnosis of Ebstein's anomaly, established on a previous hospital admission, was admitted to the Cook County Hospital on July 27, 1959. There were symptoms of exertional fatigue and dyspnea, but cyanosis was not present. Preoperative catheterization data demonstrated no significant intracardiac shunting, although an interatrial communication was demonstrated by passage of the catheter from the right to the left atrium. The mean right atrial pressure was 8 mm. Hg.

On July 30, 1959, a side-to-end SVC-RPA anastomosis was performed (Fig. 5). At no time was the blood flow from the superior vena cava interrupted. Improvement in the right atrial distention was apparent, and pressures recorded in the right atrium decreased significantly after completion of the shunt. The child's postoperative course was uneventful.

Two months after operation, the child was improved symptomatically, and x-ray studies showed a decrease in heart size (Fig. 6). The electrocardiograms were unchanged in regard to evidence of right atrial hypertrophy.



A. B.

C.

Fig. 6.—Case 3. Roentgenograms of the chest taken before, 2 months after, and 8 months after SVC-RPA anastomosis. C, Heart is somewhat larger than on film *(B)* of Oct. 5, 1959, although still smaller than on preoperative roentgenogram *(A)*.

On admission for restudy 6 months after operation, improvement in the preoperative symptoms was again noted. Heart size was increased, however, almost to its preoperative dimensions and, on cardiac catheterization, the right atrial pressure was essentially the same as before operation (Fig. 7). A significant left-to-right shunt at the atrial level was demonstrated. Closure of the atrial septal defect is also being considered in this child.

CASE 4.—An 18-year-old male was admitted to the Presbyterian-St. Luke's Hospital on Feb. 9, 1960, with a history of progressive exertional dyspnea and fatigue and significant retardation of growth and development. Clinical findings were consistent with a diagnosis of Ebstein's anomaly. Cardiac catheterization data obtained on this patient from another hospital demonstrated an elevation of right atrial pressure, with a mean of 8 mm. Hg, and confirmed the displacement of the tricuspid valve. Peripheral arterial oxygen saturation was normal, and no evidences of an interatrial communication were found.

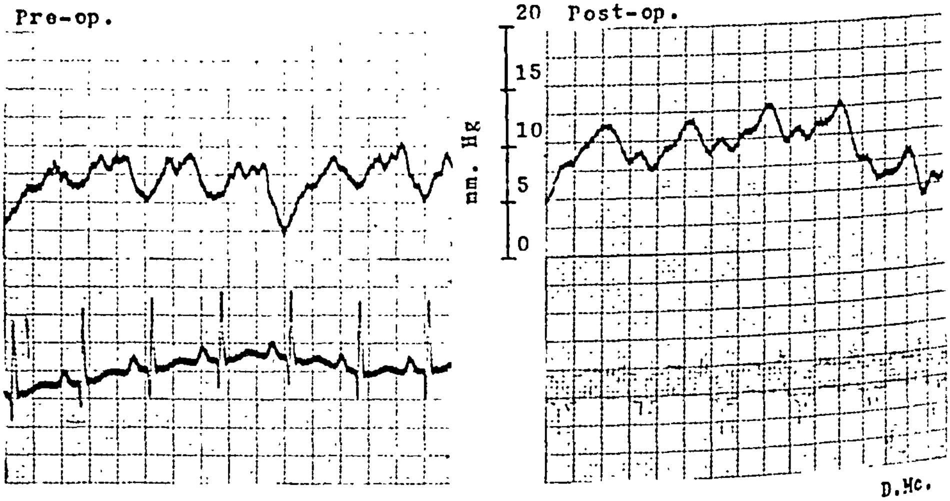


Fig. 7.—Case 3. Right atrial pressures recorded at cardiac catheterization before and 6 months after SVC-RPA anastomosis, which demonstrate equivalent levels of pressure and similar pressure-pulse contours.

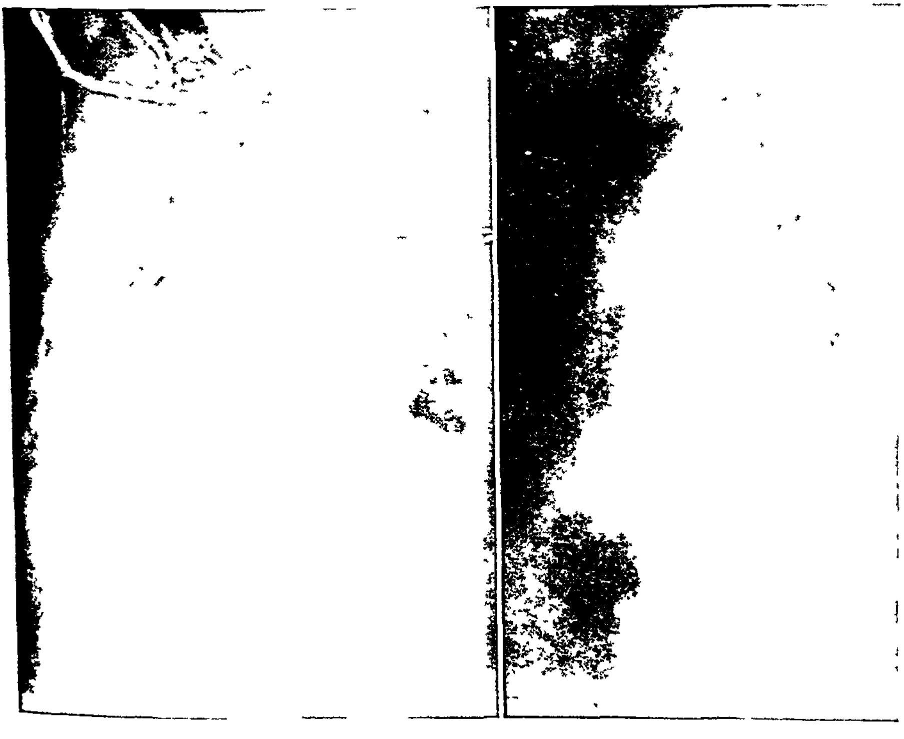
A side-to-end SVC-RPA anastomosis was performed on Feb. 18, 1960, without interruption of blood flow from the superior vena cava. At the operating table, a decrease in right atrial distention was noted, and a decrease in right atrial pressure was recorded after completion of the anastomosis. The patient was discharged on the tenth postoperative day after an uneventful course.

He was readmitted 2 weeks later with a massive right hemothorax. The blood was removed by thoracentesis and did not reaccumulate. He has since been well, with gradual improvement in exercise tolerance over his preoperative status. The heart size was unchanged according to roentgenograms made 2 weeks after clearing of the hemothorax, an interval too short to allow accurate evaluation. The electrocardiogram is unchanged from its preoperative appearance. He is to be restudied within the next several months.

DISCUSSION

The experience reported here, although obviously limited, has pointed out to us certain features of the technical conduct of the operation, and has allowed us to draw a few conclusions in regard to the influence of the shunt upon the hemodynamics of these anomalies. In regard to the performance of the procedure, we are particularly indebted to Dr. William Glenn of Yale University for his personal communications to us, confirming some of our own observations, and adding others resulting from his considerably greater laboratory and clinical experience with the procedure.

Performance of either an end-to-end or side-to-end superior vena cava-distal right main pulmonary artery anastomosis is not a difficult procedure, and has been described by Glenn,[2, 3] Robicsek and Sanger,[6] and others,[5] along with an adequate physiologic background, so that no repetition of these details is necessary here. We have used only a right anterolateral thoracotomy and would prefer this approach. Others, however, have found a sternal splitting incision satisfactory and perhaps even preferable in their hands.[4] We are emphatic in our opinion that the end-to-end anastomosis, requiring a period of occlusion of the superior vena cava, should not be done. It is our impression from postoperative angiocardiographic studies that stricture formation at the site of anastomosis is more likely to occur with the end-to-end technique, as demonstrated in 1 patient with tricuspid atresia in whom progressive signs of superior vena cava obstruction developed over a 2-month postoperative interval (Fig. 8). More impressively, the petechiae and evidences of brain injury exhibited by one



A B

Fig. 8.—*A* and *B*, Angiocardiograms which show end-to-end anastomosis of superior vena cava and distal right main pulmonary artery in 7-month-old infant with tricuspid atresia. Blood flow into right lung appears adequate, but stricture at site of anastomosis is apparent, and infant had progressive signs of superior vena caval obstruction.

child (Case 2) in the immediate postoperative period indicate that even short intervals of superior vena caval occlusion, 12 minutes in this instance, may be poorly tolerated occasionally. The side-to-end anastomosis may be performed without interruption of superior caval flow and has the added advantage of easy adaptation to a discrepancy in the transverse diameters of the two vessels to be joined together.

The effectiveness of the shunt in achieving palliation in these patients is still open to question, despite the disappearance of cyanosis and developmental gains in one child (Case 1) and the symptomatic improvement in all of the surviving patients. There has been a significant elevation of peripheral arterial oxygen saturation in the previously cyanotic child but, in each of the patients recatheterized, right atrial pressures have returned to or near their preoperative levels, and the electrocardiograms continue to show marked right atrial hypertrophy. Distention of the right atrium persists on the angiocardiogram. The catheterization data indicate that the increments of blood removed from the right atrium by the shunt have been replaced by blood flow through the atrial septal defect from the left atrium. It would seem to be a reasonable assumption that closure of the atrial septal defect is indicated in these patients and, in the future cases, should accompany performance of the anastomosis.

Despite the fact that our data is as yet inconclusive, the apparent physiologic soundness of this procedure, as it applies to Ebstein's anomaly and hypoplasia of the right ventricle, is such that further clinical trial is justified in carefully selected patients with severe and progressive symptoms in whom no other form of treatment is effective.

SUMMARY

Case reports are presented of 1 patient with congenital hypoplasia of the right ventricle and 3 patients with Ebstein's anomaly, in whom superior vena cava-distal right main pulmonary artery anastomoses were performed. In all patients a decrease in right atrial pressure was recorded at the operating table. Symptomatic improvement has been achieved in the 3 surviving patients and, in 1 child who was cyanotic before operation, cyanosis is now absent. In the 2 children studied by cardiac catheterization before and after operation, right atrial pressures have returned to or near the preoperative levels, due to left-to-right shunting through atrial septal defects.

A side-to-end rather than an end-to-end anastomosis is preferred, since the latter technique requires temporary occlusion of the superior vena cava, exposing the patient to the possibility of cerebral injury. Stricture formation at the site of anastomosis may be more likely with the end-to-end anastomosis.

Follow-up studies are incomplete, but further clinical trial of the superior vena cava-distal right main pulmonary artery anastomosis, accompanied by closure of the atrial septal defect when that additional anomaly is present, appears justified in severely disabled or deteriorating patients with Ebstein's anomaly or hypoplasia of the right ventricle.

REFERENCES

1. Gasul, B M, Weinberg, M., Jr., Luan, L. L, Fell, E H., Bicoff, J. P., and Steiger, Z: Superior Vena Cava Right Main Pulmonary Artery Anastomosis: Surgical Correction for Patients With Ebstein's Anomaly and for Congenital Hypoplastic Right Ventricle, J. A. M. A 171: 1797, 1959.
2. Glenn, W. W. L, and Patino, J. F.: Circulatory Bypass of Right Heart. I Preliminary Observations on Direct Delivery of Vena Caval Blood Into Pulmonary Arterial Circulation: Azygos Vein Pulmonary Artery Shunt, Yale J. Biol Med. 27: 147, 1954
3. Glenn, W. W. L: Circulatory Bypass of Right Side of Heart, New England J. Med. 258: 117, 1958.
4. Glenn, W. W. L: Personal communication.
5. Nuland, S. B, Glenn, W. W. L, and Guilfoil, P. H.: Circulatory Bypass of the Right Heart, Surgery 43: 184, 1958
6. Robicsek, F., and Sanger, P.: Vena Cava–Pulmonary Artery Anastomosis for Vascularization of the Lung, J. THORACIC SURG 35. 440, 1958

DISCUSSION

DR WILLIAM W. L. GLENN, New Haven, Conn —As pointed out in our initial report on the vena cava pulmonary artery procedure, this type of shunt as shown in the first slide (slide) is applicable to any condition characterized by malfunction of the right side of the heart, provided there is no obstruction to flow through the shunt, due either to anastomosis that is too small or an increased pulmonary arterial resistance

We have now employed the caval pulmonary artery procedure in 6 patients. The first of these patients is now more than 2 years postoperative

This slide demonstrates the condition of these patients pre and postoperative. All patients are markedly benefited by the procedure, corresponding to the increased arterial oxygen saturation The 2 patients with tricuspid atresia were both infants The 2 patients with tetralogy of Fallot deserve special mention We believe that the Blalock or Potts procedure is entirely satisfactory in the young patient and that the corrective procedure is indicated in the older patient. However, these 2 patients had unusual conditions complicating the tetralogy of Fallot One patient was a 41 year old woman with congenital complete heart block and the second was a 6 year old child with multiple constrictions of the pulmonary artery, clearly shown in the preoperative angiocardiogram No further procedure is contemplated in either patient at the present time, although if a corrective procedure were decided on at a later date, it would not be necessary to in any way disturb the vena cava pulmonary artery shunt.

This procedure is a satisfactory one for several reasons First, it provides for the direct delivery of venous blood to the lungs, second, the work of the left side of the heart is not increased, and third, the work of the right side of the heart is lessened

We are very appreciative of Dr Weinberg's demonstration that if the atrial defect is left open in the treatment of Ebstein's anomaly with the vena cava pulmonary artery procedure, one may then change a predominantly right to left shunt to a left to right shunt. We have 1 patient with Ebstein's anomaly whose major shunt is predominantly left to right, but in most of these patients it is right to left

DR FREDERICK H. TAYLOR, Charlotte, N C —We certainly enjoyed Dr. Weinberg's presentation very much—primarily, I suppose, because we agree with him, in that we feel that this is the operation of choice for tricuspid atresia

Our group in Charlotte has been interested in this operation since 1954, when Dr Robicsek described it. We believe it can be extended beyond these criteria noted by Dr. Weinberg, such as in certain tetralogies in the very young who are quite cyanotic It is simple in that no pump system is required

(Slide) This is a case of a boy who had transposition with pulmonary stenosis. (Slide) That's the preoperative angiogram and the postoperative angiogram, which show the increased vascularity from this anastomosis. This child, 2 years postoperatively, has obliged us by standing on his head for prolonged periods of time, and has shown good flow from the superior caval drainage. (Laughter)

This slide simply shows the increase in venous pressure during temporary occlusion of the vena cava for anastomosis and a return not to base line but a slightly elevated level. We do the end-to-end anastomosis, leaving the azygos vein open until the anastomosis is completed and then divide the azygos vein.

DR. WEINBERG (Closing).—I would like to thank Dr. Glenn and Dr. Taylor for their remarks, as well as for their original work, which helped us to formulate the therapy in these patients.

MYOCARDIAL INFARCTION IN INFANCY

The Surgical Management of a Complication of Congenital Origin of the Left Coronary Artery From the Pulmonary Artery

David C. Sabiston, Jr., M.D., Salvatore Pelargonio, M.D. (by invitation), and Helen B. Taussig, M.D. (by invitation), Baltimore, Md.*

Myocardial infarction in infancy is an uncommon condition but is being recognized during life with increasing frequency. In the majority of instances this finding is the result of a congenital lesion in which the left coronary artery arises from the pulmonary artery. In 1911, Abrikossoff[1] described the first case of this type and, recently, Keith[2] has reported a group of cases together with over 50 additional ones from the literature. In this malformation the left coronary artery arises from the pulmonary artery, a vessel which contains blood of diminished oxygen saturation and of low pressure. Infarction of the left ventricle usually occurs within the first several months of life and is associated with an extremely high mortality. Previous discussions of this subject in the literature have directed attention to the dynamics of blood flow in the anomalous left coronary artery and to the pathogenesis of the myocardial infarction which characteristically occurs. These points, as well as the therapeutic approach to this problem, have remained controversial. The purpose of this communication is to present a review of the clinical and pathologic findings in 12 patients with this condition. In this group of patients, investigative studies have been performed on postmortem specimens and at the time of operation. Particular attempts have been made to determine the anatomic features of the left and right coronary arteries and the collateral vessels between them. Injection and perfusion studies were done in an effort to determine the direction of blood flow in the anomalous coronary artery, and arterial pressure and oxygen saturation determinations were done to establish (conclusively) this point. These findings have been utilized in an attempt to formulate a rational approach to the therapy of this condition.

CLINICAL DIAGNOSIS

In the majority of infants with anomalous origin of the left coronary artery from the pulmonary artery, the physical examination at birth is essentially nor-

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*Investigator, Howard Hughes Medical Institute.

mal and the child continues without evidence of a serious malformation for the first several weeks of life. Nevertheless, symptoms may appear at birth in a small number with rapid progression. In the present series, 2 infants were symptomatic at birth and all infants were ill by the age of 3 months.

Symptoms.—In most instances the first abnormality noted is rapid and difficult respiration. This may progress to wheezing, coughing, and panting. In the more severe cases, cyanosis is present. It has also been noted that some infants show evidence of anginal pain, particularly during and after feeding. Often vomiting occurs and attacks of sweating, pallor, and dyspnea are a characteristic feature of this malformation. In many instances a history of recurrent respiratory infections is obtained. Such infections tend to become more severe and more refractory to treatment with succeeding attacks.

Physical Findings.—On examination the infant may appear either acutely or chronically ill. Respiratory difficulty is usually prominent with a rapid rate and use of the accessory muscles. Moist râles may be present and cyanosis of the lips and nail beds may accompany the more severe cases. Examination of the chest reveals marked cardiac enlargement. In most instances no murmur is audible, although a systolic murmur is at times heard over the precordium, particularly along the left sternal border. It should be noted that associated intracardiac defects may be present, and under these circumstances the murmur characteristic of the cardiac defect is heard. Enlargement of the liver is a consistent finding and the spleen is often palpable. In a small group of patients the presenting picture may be that of shock associated with the findings of acute myocardial infarction. Marked tachycardia, hypotension, and peripheral vascular collapse characterize this form of the condition.

Fluoroscopy and Chest Film.—The heart is massively enlarged involving chiefly the left atrium and left ventricle. The left cardiac border frequently extends to the lateral rib margin and the pulsations of the left ventricle are markedly diminished (Fig. 1, *A* and *B*). The pulmonary vascular markings are often increased.

Electrocardiogram.—The electrocardiogram is usually characteristic, and the changes closely simulate those associated with myocardial infarction in the adult. The heart rate is rapid. In the standard leads, T_1 and T_2 are usually inverted and the S-T segment in Lead I is slightly raised. The T waves in the precordial leads V_5 and V_6 are usually inverted and deep Q waves are often present. Additional changes may be present and these findings are classically reviewed in a recent publication by Keith.[2]

Angiocardiography.—Injection of radiopaque dye into the right heart demonstrates a normal right atrium and right ventricle. The pulmonary vascularity may be slightly increased, but the striking feature is the massive enlargement of the left atrium and left ventricle. The latter is usually tremendous and has a very thin wall. The contrast medium may linger for a prolonged period in the left heart, indicating a sluggish circulation secondary to a failing left ventricle. It is rare for the anomalous left coronary artery to be filled from the pulmonary artery during angiocardiography (Fig. 1, *C*).

Aortography.—The injection of dye directly into the aorta with filling of the proximal aorta usually demonstrates the right coronary artery with a normal origin. This vessel is often larger than normal and a communication by collateral vessels with the left coronary artery may be clearly demonstrated as has been shown by Morrow and associates.[3]

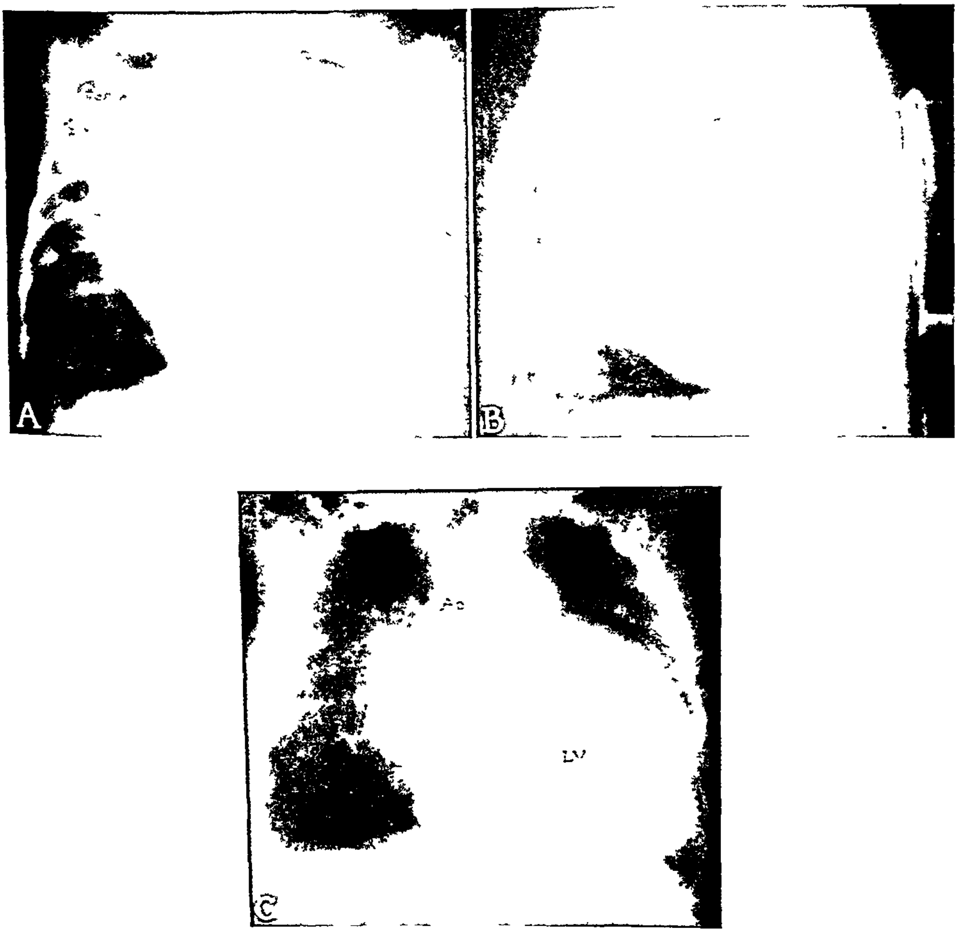

Fig. 1.—*A*, Chest film which illustrates marked cardiac enlargement with extension of left cardiac border to the axillary line. *B*, Lateral view of *A*. *C*, Angiocardiogram which demonstrates marked enlargement of the left ventricle. The dye can be seen to extend almost to the axillary line, indicating that the left ventricular wall is quite thin.

Cardiac Catheterization.—There are few reports of cardiac catheterization available in patients with anomalous origin of the left coronary artery from the pulmonary artery. However, in those described, some of the findings include: (1) a low mixed venous saturation in the right heart, (2) elevation of the pulmonary arterial pressure, and (3) elevation of the pulmonary wedge pressure. The changes essentially represent left ventricular failure.

A diagnosis of anomalous origin of the left coronary artery from the pulmonary artery with left ventricular myocardial infarction was made, and the child was digitalized. An improved flow of oxygenated blood through the anomalous coronary artery by means of a pulmonary-aortic anastomosis was attempted but was unsuccessful, and the child died one hour after operation. At autopsy, an anomalous left coronary artery arising from the pulmonary artery was found. Massive scarring with focal calcification was present in the left ventricle and in the interventricular septum.

CASE 8.—This 2-month-old female was admitted with a history of difficult breathing and vomiting. On physical examination the respiratory rate was 60 and the infant was obviously acutely ill and appeared to be in peripheral vascular collapse. The heart was markedly enlarged. No murmurs were heard. A gallop rhythm was present. The liver was palpated 3 cm. below the right costal margin. The blood pressure was repeatedly found to be quite low, with a maximum of 80 mm. Hg systolic being obtained. The child's condition was critical and the hypotension persisted.

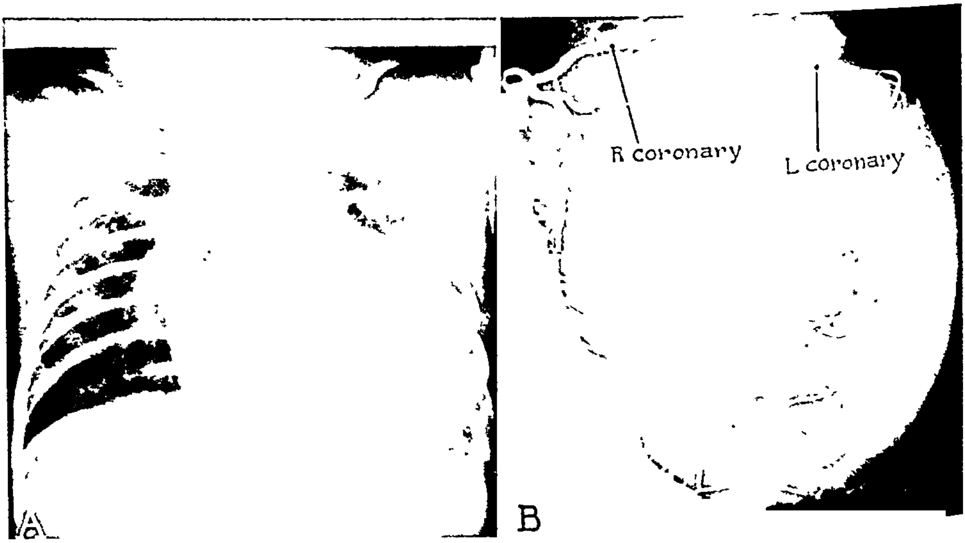

Fig. 2.—*A*, Chest film which shows marked cardiac enlargement (Case 11). *B*, Injection of heart shown in chest film at postmortem examination. Cannulae have been placed in the right coronary and left coronary arteries. The cannula in the left coronary artery extends into the anterior descending branch. Diodrast was injected into the right coronary artery and communications between it and the left coronary artery with filling of the anterior descending and circumflex branches is easily seen The dye appeared in the pulmonary artery at the orifice of the anomalous left coronary artery. It is interesting that the left coronary arterial system filled prior to entry of the dye into the venous system.

Electrocardiogram: Sinus rhythm with rate of 160. S-T segments elevated in V_5, V_6, and V_7. T waves inverted in Lead I and V_6. Q wave present in Lead I and aV_L.

The infant was placed in oxygen and given digitalis. It was necessary to begin an intravenous infusion of metaraminol bitartrate (Aramine). The arterial pressure rose from 70/30 to 90/70 mm. Hg with a concomitant improvement in the general appearance. On several occasions an attempt was made to discontinue the intravenous administration of vasopressor but, in each instance, the blood pressure promptly fell to shock levels. Increasing amounts of Aramine became necessary in order to maintain the arterial pressure, and it was decided that the condition was hopeless unless a surgical procedure could offer benefit. Accordingly, one week following admission, the left chest was opened and the heart was found to be massively enlarged with infarction of the left ventricle. The child's blood pressure fell to unrecordable levels accompanied by a marked bradycardia. It was apparent that the situation was desperate. However, the left coronary artery was dissected and was found to arise from the left pulmonary artery. It was ligated and the heart action became improved temporarily, but the heartbeat ceased shortly thereafter and could not be resuscitated. Postmortem examination revealed an anomalous left coronary artery arising from the pulmonary artery with infarction of left ventricle (Fig. 3, *A*).

CASE 9.—This 2-month-old infant was admitted with a history of difficult respirations and with a feeding problem. An examination at the end of the first month of life was said to be normal. At the age of 6 weeks the child suddenly became dyspneic while feeding. On examination the heart was enlarged to the anterior axillary line and the sounds were distant. A Grade 2, slightly harsh systolic murmur was heard along the left sternal border and radiated over the precordium. The liver was palpable 1.5 cm. below the right costal margin, and the spleen was felt 2 cm. below the left costal margin.

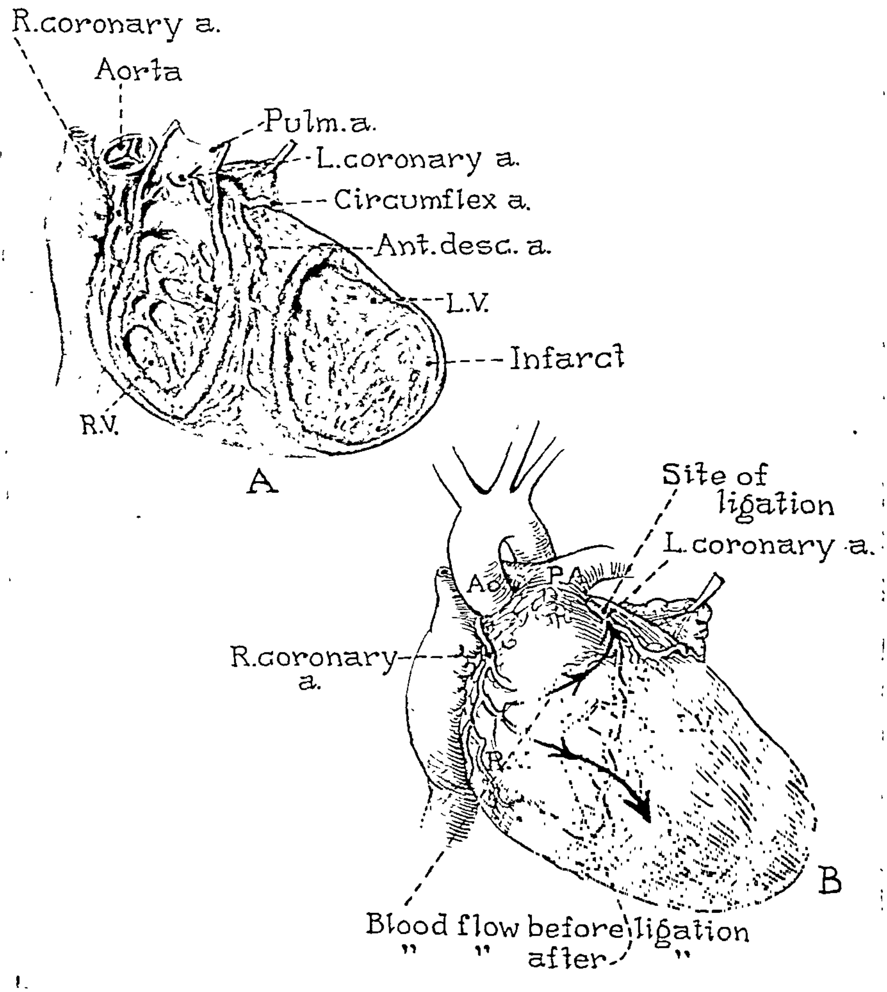

Fig. 3.—*A*, Specimen obtained at the time of postmortem examination (Case 8). The left coronary artery arises anomalously from the pulmonary artery. The dilated left ventricle with aneurysmal area of infarction is seen.

B, Diagrammatic illustration of blood flow in the anomalous left coronary artery before and after ligation at its origin. Prior to ligation the blood flowed from the aorta under systemic arterial pressure (with complete oxygen saturation) into the right coronary artery and through collateral vessels into the left coronary artery with ultimate drainage into the pulmonary artery in a *retrograde* manner. Following ligation of the anomalous left coronary at its origin, the arterial blood from the right coronary artery is directed peripherally into the branches of the left coronary artery where it reaches the myocardial vascular bed.

Electrocardiogram: Sinus rhythm with rate of 140. QRS duration 0.05. Deep Q waves in Lead I, aV_R, aV_L, V_4, and V_5. S-T segment elevation in V_5 and V_6. T waves inverted in V_5 and V_6.

Fluoroscopy and chest films revealed marked cardiomegaly. A cine angiocardiogram (taken at the Memorial Hospital of the University of North Carolina) revealed a small right heart with a massively dilated left ventricle. The left ventricular wall was thin and pulsations were barely discernible. There was no evidence of filling of the left coronary artery from the pulmonary artery. A diagnosis of anomalous origin of the left coronary artery from the pulmonary artery with myocardial infarction was made.

At thoracotomy the heart was found to be massively enlarged. There was a large infarct on the anterolateral surface of the left ventricle. The pulsations in this region were paradoxical and the myocardium quite thin (Fig. 4, *A*). The left coronary artery arose from the pulmonary artery. It was dissected at its origin and was found to be of normal size. Its anterior descending and circumflex branches were visualized (Fig. 4, *B*). The mean pressure in the left coronary artery was measured and found to be 30 mm. Hg (Fig 6, *A*). An arterial clamp was then applied to the artery at its origin from the pulmonary artery and the pressures in the left coronary artery were again measured. With occlusion of the left coronary at its origin, the pressure distal to the clamp was 75 mm. Hg. A simultaneous mean pressure in the pulmonary artery was 25 mm. Hg. Blood drawn from the anomalous left coronary artery for oxygen content was found to be 100 per cent saturated while a simultaneous sample from the pulmonary artery was found to have a saturation of 76 per cent (Fig. 6, *B*). These observations demonstrated conclusively that blood flow in the anomalous coronary artery was *retrograde* into the pulmonary artery (Fig. 3, *B*). The anomalous left coronary was then ligated close to the pulmonary artery with three silk sutures. The pericardium was removed and concentrated phenol (88 per cent) was applied to the entire surface of the upper epicardium. Postoperatively the child made an uneventful recovery.

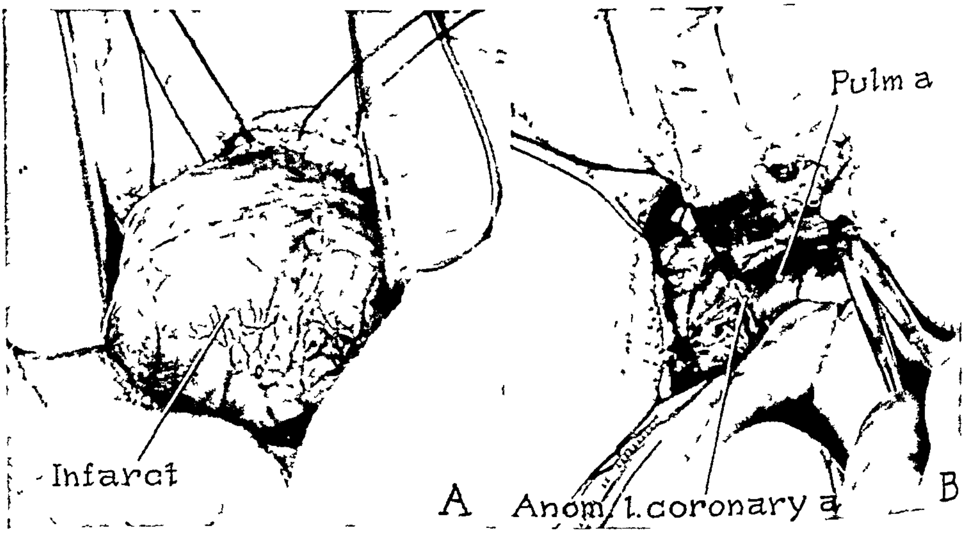

Fig. 4.—*A*, Photograph of heart at the time of operation. The area of infarction of the left ventricle is seen. This portion of the ventricle contracted paradoxically with the beat of the heart.

B, Photograph which illustrates operative dissection of the left coronary artery at its origin from the pulmonary artery. Two ligatures are shown and a third was subsequently placed. The vessel was ligated at its origin proximal to the branching of the anterior descending and circumflex branches.

A recent report from the attending cardiologist, approximately one year following operation, states that the child is developing normally. The electrocardiogram shows less evidence of myocardial ischemia and the heart is somewhat smaller on the chest film. The child is essentially asymptomatic.[4]

CASE 10.—This 3-month-old Negro female was admitted with a history of difficult breathing which was first noted at the age of 6 weeks. Shortly thereafter a cough appeared and the dyspnea became more pronounced. On examination the child was acutely ill with a respiratory rate of 70. The cardiac sounds were of poor quality and no murmurs were heard. Fluoroscopic examination and chest films revealed a markedly enlarged heart, chiefly involving the left ventricle.

Electrocardiogram: Sinus tachycardia with rate of 180. Q wave in Lead I with inversion T waves in Leads I, II, and III. T waves in V_1 and V_3 upright. T waves in V_5 and V_6 inverted.

An angiocardiogram showed normal filling of the right atrium and right ventricle. The left ventricle was greatly dilated. A diagnosis of anomalous origin of the left coronary artery from the pulmonary artery was made and operation was elected.

On Feb. 17, 1958, a left thoracotomy was performed. The left ventricle was markedly enlarged and an obvious infarct was present on the anterolateral wall. Here the myocardium was scarred and thin, and this area contracted paradoxically. The pressure in the left ventricle was found to be 120/40 mm. Hg. The marked elevation in diastolic pressure was impressive and reflected the failing left ventricle. The pericardium was excised and concentrated phenol (88 per cent) was applied to the entire surface of the epicardium. The thymus gland and fatty tissue in the mediastinum was sutured over the surface of the left ventricle. The postoperative course was entirely uneventful.

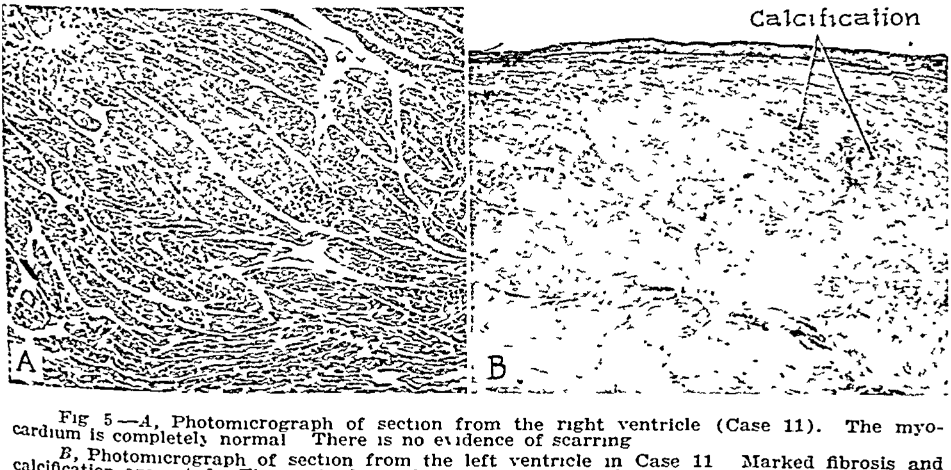

Fig 5—*A*, Photomicrograph of section from the right ventricle (Case 11). The myocardium is completely normal There is no evidence of scarring

B, Photomicrograph of section from the left ventricle in Case 11 Marked fibrosis and calcification are noted. The ventricle in this area was quite thin and the site of an infarction measuring 4 cm in diameter

Since discharge the child has had several attacks of upper respiratory infections, but otherwise has remained well. The cardiomegaly persists, as do changes in the electrocardiogram, indicating myocardial ischemia. However, the child is considerably improved over the preoperative status.

CASE 11.—This 3-month-old Negro male was admitted with a history of marked dyspnea. On examination the temperature was 39.6° C., pulse 200, and respirations 110. The blood pressure was not obtainable. The infant was obviously acutely ill and almost moribund. Respiratory distress was marked. The heart was markedly enlarged. No murmurs were heard. The liver was palpable 3 cm. below the right costal margin. Fluoroscopic and x-ray examination showed a markedly and symmetrically enlarged heart (Fig. 2, *A*).

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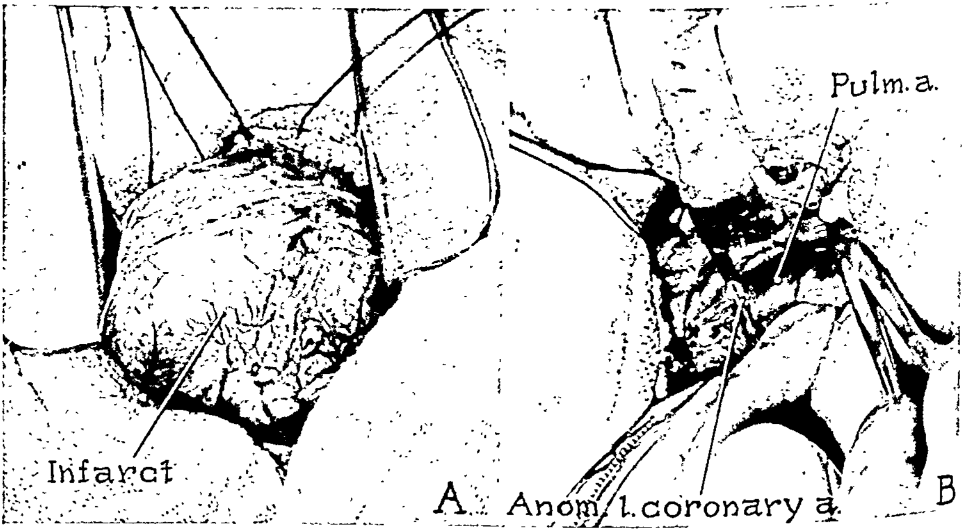

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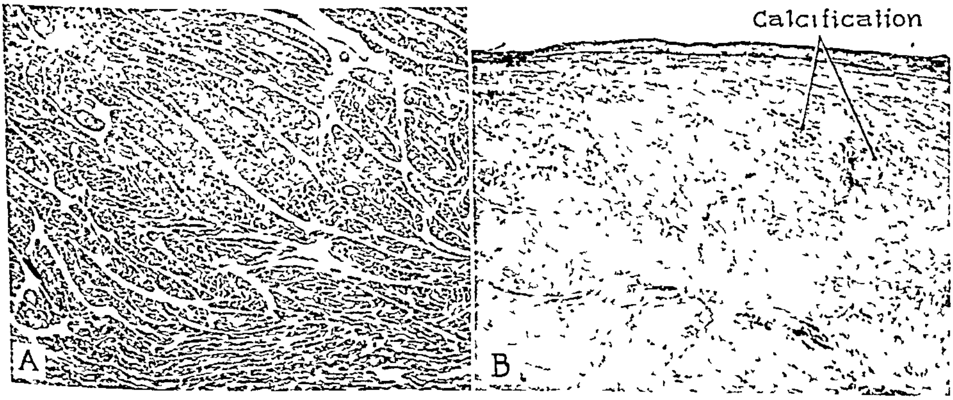

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Electrocardiogram: Sinus tachycardia with rate of 170. S-T segment elevated in V_5 and V_6. T waves inverted in V_5 and V_6

The infant was placed in oxygen and digitalized which produced considerable improvement. The child was later discharged but readmission was necessary because of the reappearance of cardiac failure. An angiocardiogram demonstrated a small right atrium and right ventricle. The dye passed freely through the pulmonary circulation into a large left ventricle with a very thin wall. A diagnosis of anomalous origin of the left coronary artery from the pulmonary artery was established.

On Sept 10, 1956, a left thoracotomy was performed. At this time the child was 8 months of age. Immediately upon opening the pericardium the heart entered ventricular fibrillation and it was never possible to restore a normal beat. The anterior surface of the left ventricle was involved in a massive infarct with a thin, fibrous wall. Postmortem examination revealed an anomalous left coronary artery arising from the pulmonary artery and a large left ventricular infarct (Figs. 2, *B*, and 5).

CASE 12.—This female infant was admitted with the history of easy fatigability and difficulty during feeding. Labored respiration and a cough had also been noted. On examination the lips and nail beds were cyanotic. The heart was markedly enlarged and no murmurs were heard. Fluoroscopic examination and chest films revealed a markedly enlarged heart.

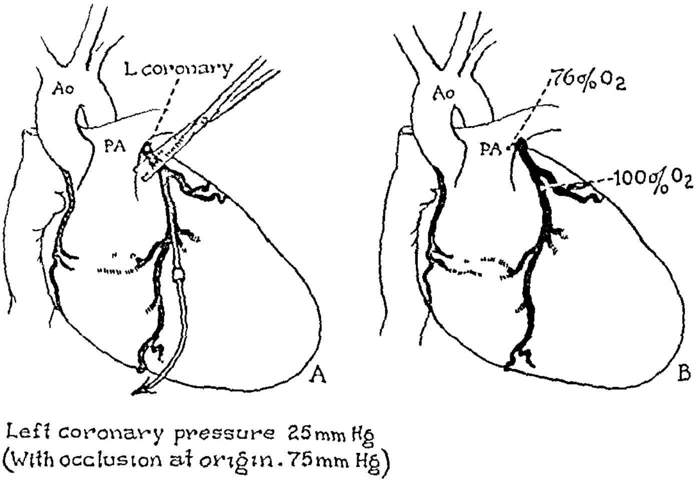
L coronary
Ao
PA
A
Left coronary pressure 25mm Hg
(With occlusion at origin. 75mm Hg)
Ao
76% O2
PA
100% O2
B

FIG 6.—*A*, Diagrammatic illustration of the pressure in an anomalous left coronary artery. The mean pressure in this vessel was found to be 30 mm Hg. With occlusion of the vessel at its origin from the pulmonary artery with an arterial clamp, the systolic pressure rose to 75 mm Hg. A simultaneous mean pressure in the pulmonary artery was 25 mm Hg. These determinations demonstrate that the blood in the anomalous left coronary artery was supplied by the right coronary artery through anastomotic collateral channels.

B, Diagrammatic illustration of determination of oxygen saturation in anomalous left coronary artery. Blood withdrawn from this vessel had an oxygen saturation of 100 per cent while a simultaneous sample from the pulmonary artery had an oxygen saturation of 76 per cent. These figures indicate that the blood in the anomalous coronary artery does not arise from the pulmonary artery, but is supplied from the right coronary artery.

Electrocardiogram: Sinus tachycardia with rate of 180. S T segment elevated in V, and T waves inverted in V_1, V_5, and V_6. Q waves in V_1, V_3, and V_6.

An angiocardiogram demonstrated a tremendous left ventricle with a thin wall. The left ventricular contraction was poor. A firm diagnosis of anomalous origin of the left coronary artery from the pulmonary artery with left ventricular myocardial infarction was made.

On Sept 21, 1956, a left thoracotomy was performed. On entry into the pericardium a moderate amount of free fluid was present. The left ventricle showed a large infarct. This area of the heart was quite fibrotic and thin. It contracted paradoxically with the beat of the heart. The pericardium was removed and a concentrated solution of phenol (88 per cent) was applied to the entire epicardial surface. The left lung was sutured to the surface of the left ventricle. The postoperative course was uneventful.

Since discharge she has been seen on several occasions for follow-up examinations and has developed normally. Cardiomegaly and electrocardiographic evidence of myocardial ischemia persist, but the child is now 4 years of age and appears otherwise normal.

DISCUSSION

Although it may appear somewhat paradoxical, myocardial infarction in infancy is recognized as a definite clinical entity and is being discovered during life with increasing frequency. Death from myocardial infarction in this age group has been reported following calcification of the coronary arteries,[5, 6] thrombosis of coronary arteries without calcification,[7] and in association with anomalous origin of the left coronary artery from the pulmonary artery.[2, 8] The latter condition is considered to be the most common of this group. In 1911, Abrikossoff[1] reported the first case of anomalous origin of the left coronary artery from the pulmonary artery. This description stimulated little interest until Bland, White, and Garland[9] first described diagnostic features of this condition in the electrocardiogram of an infant with this diagnosis. Since that time increasing interest has been shown in the malformation, and a number of cases and clinical studies have been reported. Recently Keith has published an excellent review of his cases, together with those previously reported, bringing the total number to nearly 60.[2]

The pathogenesis of the left ventricular myocardial infarction in patients with anomalous origin of the left coronary artery from the pulmonary artery has attracted considerable attention and speculation. It has been the opinion of some that the left ventricle becomes infarcted as a result of the perfusion with blood of a low oxygen saturation and under a low pressure. This is explained by the fact that the normal pressure in the pulmonary artery is considerably lower than that in the aorta and that the oxygen saturation of the blood within it is also low. However, a recent review of an early report by Brooks,[10] published in 1886, has stimulated a new approach. This anatomist reported two instances of anomalous origin of the *right* coronary artery from the pulmonary artery. These cases occurred in adults and were found incidentally in cadavers in the dissecting laboratory. He made the observation that extremely large arterial communications were present between the branches of the anomalous right coronary artery and the normal left coronary artery. Since the pressure in the pulmonary artery was quite low, he concluded that under these circumstances blood in the right coronary artery must flow in a *retrograde* manner. It was his concept that blood entered the left coronary artery from the aorta under high pressure and passed through collateral vessels into the right coronary artery with ultimate drainage into the pulmonary artery. No infarction was described in either of these cases and indeed it is a well-known fact that many instances of anomalous origin of the right coronary artery from the pulmonary artery have been described which are asymptomatic and unassociated with pathologic changes. This concept also gained the support of Maude Abbott[11] and, more recently, Edwards[12] has added further evidence for this explanation. He has emphasized the fact that low oxygen saturation alone is unlikely to produce ischemia, inasmuch as many patients with congenital cyanotic heart disease have far lower oxygen saturation in the coronary arteries than exists in the pulmonary artery. Apley and associates[13] have reported that at the time of operation bright red blood was noted to flow freely from the distal end of an anomalous left coronary, indicating that it originates from an arterial source. Case and associates[14] have performed injection studies on specimens at postmortem examination and have demonstrated free communication between the left and right coronary arteries.

In the studies reported in the present communication, attention has been directed to the observations made during perfusion of the right coronary artery at the time of postmortem examination. Contrast medium injected into the right coronary artery freely crossed into the left coronary artery through easily visible collateral vessels (Fig. 2, *B*). This indicates that the path of least resistance is through the collateral channels between the right and left coronary circulation in preference to an initial route into the coronary venous bed (Fig. 3). Following injection, the dye ultimately appeared in the pulmonary artery at the orifice of the anomalous left coronary artery. In a second study performed at the time of operation (Fig. 4), it was demonstrated that the blood in the anomalous left coronary artery is arterial and with an oxygen saturation of 100 per cent (Fig. 6, *B*). Furthermore, the pressure in this vessel rose appreciably when the left coronary artery was occluded at its origin (Fig. 6, *A*). These data conclusively demonstrate that the blood in the anomalous left coronary artery flows in a *retrograde* direction, and that blood entering the right coronary artery from the aorta passes through collateral vessels into the left coronary artery with ultimate drainage into the pulmonary artery. Under these circumstances, it is apparent that arterial blood is being drained away from the left ventricle despite the fact that this oxygenated blood is greatly needed by the myocardium. This fact led Edwards[12] to suggest that ligation of the left coronary artery at its origin might significantly improve the circulation to the left ventricle. This was first performed by Mustard in 1956, but the child died suddenly 8 hours after operation.[15] Jahnke[16] performed this procedure on a 4-month-old infant and, although the child did well in the immediate postoperative period, she died 2 months later in cardiac failure. Davis[17] has performed ligation of the anomalous coronary artery in an infant 4 months of age with success at the time of report. Morrow[3] has recently observed an interesting case in which an anomalous left coronary artery from the pulmonary artery was proved by aortography and later at operation. A ligation of the anomalous coronary artery with de-epicardialization and cardiopneumopexy was performed. This infant has done remarkably well and one year following operation shows diminished electrocardiographic evidence of myocardial ischemia. The course of this child appears to be similar to one of the infants in the present report.

An increasing number of reports of anomalous origin of the left coronary artery from the pulmonary artery is appearing in the literature. Furthermore, it is apparent that the diagnosis is being made with increasing frequency at a time when it is possible to institute therapy. An analysis of the reported results indicates that the mortality in untreated cases is quite high and death usually occurs in the first year of life (Fig. 7). Although Kaunitz[8] collected a small number of cases of adults with this condition, the great majority of patients with this disorder do not survive beyond infancy. The diagnosis can be made with considerable accuracy by the history, physical examination, chest film, and electrocardiogram. However, in doubtful cases, angiocardiography and aortography may be employed to confirm the diagnosis.

In the past a variety of methods have been advocated in an effort to improve the circulation to the left ventricle. These procedures have included: (1) a systemic-pulmonary anastomosis in an effort to increase the oxygenation of the blood in the pulmonary artery[2]; (2) the production of an increased pressure in the proximal pulmonary artery by a constriction placed immediately distal to the origin of the anomalous coronary artery[18]; (3) the introduction of talc into the pericardial cavity to stimulate collateral circulation and the ingrowth of new vessels into the ischemic ventricle[19]; (4) the direct anastomosis of a systemic artery to the anomalous left coronary artery[15]; (5) resection of the infarcted area in an effort to eliminate the paradoxical motion of the left ventricle[13]; and (6) ligation of the anomalous coronary artery at its origin, either alone or combined with pericardiectomy and de-epicardialization.[4] Despite these suggestions, only pericardial irritants and ligation of the anomalous coronary artery have been reported to be effective. There is little doubt that a reconstructive procedure such as the anastomosis of the anomalous coronary to a systemic vessel is the ideal approach. However, it should be noted that these

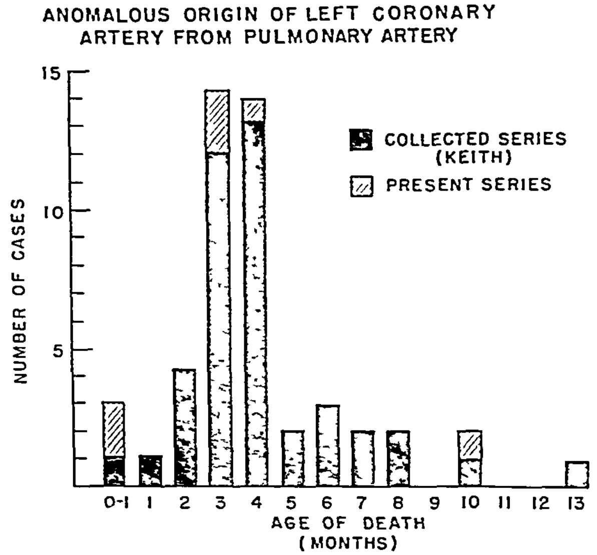

Fig 7—Comparison of age of death in present series and collected series reported by Keith

infants are almost always in an extremely poor condition and tolerate surgery poorly. The fact that every patient in the present series without surgical therapy died before the first year of life bears emphasis. Since death has occurred frequently with induction of anesthesia or shortly after the onset of the operation, a rapid and simple procedure with a minimum of dissection is most likely to be followed by survival. Strong emphasis should be placed upon the importance of early diagnosis and treatment before irreversible infarction occurs. At the present it appears that ligation of the anomalous left coronary artery at its origin combined with pericardiectomy and de-epicardialization offers the greatest chance for survival and improvement. The favorable course of 3 of 5 infants treated by one or both of these methods in the present report supports this view.

SUMMARY

Myocardial infarction in infancy is most frequently the result of an anomalous origin of the left coronary artery from the pulmonary artery. Twelve cases are reviewed and the diagnostic, pathologic, and therapeutic aspects are presented. Emphasis is placed upon the high mortality rate in those cases managed without operation. Evidence is presented which supports the concept that the blood flow in the anomalous left coronary artery is *retrograde* and that arterial blood is actually drained away from the myocardium into the pulmonary artery. This finding is utilized in the therapeutic approach. Ligation of the anomalous left coronary artery at its origin combined with revascularization by pericardiectomy and de-epicardialization have been shown to produce encouraging results. Early diagnosis and treatment are mandatory if significant improvement is to be obtained before irreversible changes of myocardial infarction occur.

REFERENCES

1. Abrikossoff, A.: Aneurysma des linken Herzventrikels mit abnormer Abgangstelle der linken Koronararterie von der Pulmonalis bei einem funfmonatlichen Kinde, Virchows Arch. path. Anat. 203: 413, 1911.
2. Keith, J. D.: The Anomalous Origin of the Left Coronary Artery From the Pulmonary Artery, Brit. Heart J. 21: 149-161, 1959.
3. Morrow, A. G.: Personal communication.
4. Sabiston, D. C., Neill, C. A., and Taussig, H. B.: The Direction of Blood Flow in Anomalous Left Coronary Artery Arising From the Pulmonary Artery, Circulation (In press).
5. Cochrane, W. A., and Bowden, D. H.: Calcification of the Arteries in Infancy and Childhood, Pediatrics 14: 222, 1954.
6. Traisman, H. S., Limperis, N. M., and Traisman, A. S.: Myocardial Infarction Due to Calcification of the Arteries in an Infant, A. M. A. J. Dis. Child. 91: 34-37, 1956.
7. Martelle, R. R.: Coronary Thrombosis in a Five-Month-Old Infant, J. Pediat. 46: 322, 1955.
8. Kaunitz, P. E.: Origin of Left Coronary Artery From Pulmonary Artery, Am. Heart J. 33: 182, 1947.
9. Bland, E. F., White, P. D., and Garland, J.: Congenital Anomalies of Coronary Arteries: Report of an Unusual Case Associated With Cardiac Hypertrophy, Am. Heart J. 8: 787, 1933.
10. Brooks, H. St. J.: Two Cases of an Abnormal Coronary Artery of the Heart Arising From the Pulmonary Artery, J. Anat. Physiol. 20: 26, 1886.
11. Abbott, M. E.: Congenital Cardiac Disease *in* Osler, William, Modern Medicine, ed. 3, Philadelphia, 1927, Lea & Febiger, vol. 4, p. 794.

12. Edwards, J. E.: Functional Pathology of Congenital Cardiac Disease, Philadelphia, 1954, W. B. Saunders Company, Pediat. Clin. North America. vol. 1, p. 13.
13. Apley, J., Horton, R. E., and Wilson, M. G.: The Possible Role of Surgery in the Treatment of Anomalous Left Coronary Artery, Thorax 12: 28, 1957.
14. Case, R. B., Morrow, A. G., Stainsby, W., and Nestor, J. O.: Anomalous Origin of the Left Coronary Artery. The Physiologic Defect and Suggested Surgical Treatment, Circulation 17: 1062, 1958.
15. Mustard, W. T.: Cited in Keith.[2]
16. Jahnke, E. J.: Cited in Case et al.[14]
17. Davis, E. W.: Cited in Case et al.[14]
18. Kittle, C. F., Diehl, A. H., and Heilbrunn, A.: Anomalous Left Coronary Artery Arising From the Pulmonary Artery, J. Pediat. 47: 198, 1955.
19. Paul, R. N., and Robbins, S. G.: A Surgical Treatment for Either Endocardial Fibroelastosis or Anomalous Origin of the Left Coronary Artery, Pediatrics 16: 147, 1955.

DISCUSSION

DR. CLAIR BASINGER, Grand Rapids, Mich.—My associates Richard Rasmussen, Richard Meade, and I had an opportunity recently to study a 12 year old symptomatic child with a continuous murmur. She had had a number of studies, including repeated right cardiac catheterizations, and we thought we established the diagnosis with retrograde angiograms. This slide shows the origin of a single left coronary artery. It is a large artery, three to four times normal size and, as the dye fills the vessels, we find a right coronary artery coming off the left, a single coronary artery here (indicating), and there is a right coronary artery–right ventricular fistula demonstrated at this point.

This slide is an artist's drawing of the operative specimen which shows the origin of the left and single coronary artery, with the right coronary artery coming down anomalously with a fairly large right ventricular fistula. The fistula was divided at its origin, and the entire right coronary artery circulation was preserved.

We could demonstrate no electrocardiographic changes of significance during or immediately after surgery. The child's murmur has since disappeared completely and she is asymptomatic.

DR. JOSEPH GILBERT, Bethesda, Md.—At the National Heart Institute we have not had the extensive experience of Dr. Sabiston with this entity but our findings corroborate in every respect those that he has put forth this morning concerning the pathophysiology and surgical treatment of the lesion.

This slide is of an aortogram performed on a 4 month old child. Although the right opacifies immediately the left coronary artery cannot be seen until (slide) later in the film series, when it is thus demonstrated to fill in a retrograde fashion via collaterals from the right.

The child was operated upon, at which time the anomalous left coronary artery was ligated and the epicardium painted with dilute phenol. He has been followed for 14 months, has grown and developed normally, and has exhibited remarkable regression in the electrocardiographic changes, which showed an anterior infarction pattern preoperatively.

DR. WILLIAM T. MUSTARD, Toronto, Ontario.—I should like to make one comment—that is that I think it's better to have two coronaries than one.

(Slide) The operation consists of turning down the internal carotid and anastomosing it to the coronary artery. This anastomosis is quite feasible, and the internal carotid in the infant is about the same size as the coronary.

Unfortunately, as you can see from the slide, this patient didn't survive, and my other 2 patients didn't either, but I still think it's a good operation. (Laughter and applause.)

DR. LEWIS H. BOSHER, Richmond, Va.—I would like to present a case which may be of some interest and which tends to back up what Dr. Mustard has just said.

Anastomosis of the left subclavian artery to the anomalous left coronary has been suggested and previously attempted by Apreis. We encountered a 4 year old child who was still alive with this unusual condition. (Slide) This child had been treated in the hospital on numerous occasions—I think, fourteen in all—for congestive failure The child was old enough to complain of chest pain. This slide shows the large heart which the child exhibited

Aortography (slide) demonstrated a single coronary vessel coming off the aorta The left coronary is not seen

This slide is the artist's drawing of the conditions exhibited at surgery, showing a large anomalous vessel arising from the pulmonary artery. It was quite feasible to turn down the left subclavian artery and to anastomose it with the distal divided anomalous coronary artery

Unwisely, we attempted pressure studies in the patient, and the child's heart went into ventricular fibrillation We could not get the heart defibrillated until we had placed the child on the bypass, and at that time we proceeded to carry out the anastomosis

This slide shows a rather good match between the two vessels and the adequate length of the left subclavian artery Unfortunately, we could not get the child off the bypass

This slide shows the match between the vessels as exhibited at postmortem examination

(Slide) There was an infarct at the apex of the left ventricle, as shown here, (slide) and the open specimen shows the infarct, which was rather extensive We feel that this is a feasible operation, at least in older infants, if the child survives to this age I don't know how satisfactory it would be in the very young infant

DR RICHARD M PETERS, Chapel Hill, N C—I'd just like to ask Dr Sabiston one question about this very nice presentation, and that is whether he really thinks the revascularization is the important step, or whether the ligation of the anomalous coronary is really the effective therapy

DR SABISTON (Closing)—In answer to Dr Peters' question concerning the value of the epicardial revascularization procedure, I regard it as being of secondary importance Ligation of the anomalous coronary artery is the definitive part of the operation

DIAGNOSIS AND SURGICAL TREATMENT OF INTRACARDIAC MYXOMA AND RHABDOMYOMA

Rodman E. Taber, M.D., and Conrad R. Lam, M.D., Detroit, Mich.

PRIOR TO 1954 when Crafoord[1] reported the first successful removal of an intra-atrial myxoma with the use of extracorporeal circulation, primary cardiac tumors were regarded with little clinical interest. Two removals previously attempted by closed methods had been unsuccessful.[2, 3] With the development of safe and dependable open-heart surgery, it has become necessary to consider these lesions in the evaluation of the cardiac patient and to employ specific diagnostic procedures for identifying them when indicated. Removal of 19 atrial myxomas with 11 successes[4-12] have previously been reported. Two patients with right atrial myxomas and one with a cardiac septal rhabdomyoma who have undergone successful surgical treatment are the subject of this report.

Although constituting the most common type of primary intracardiac tumor, the atrial myxomas have produced widely varying clinical features which have made recognition difficult. Most of the previously recorded cases, as well as the 2 cases of myxoma in this report were thought to be other types of heart disease in the initial stages of their management. As a result, the diagnosis of primary intracardiac tumor has often been made by a process of elimination or a tumor has been encountered as an unsuspected operative finding during the course of a closed cardiac operation. In a review of 125 cardiac myxomas discovered at necropsy, Prichard[13] found 75 per cent to arise in the left atrium. This apparent preponderance in the arterial side of the heart is confirmed by the frequency of left-sided lesions (80 per cent) which have been removed surgically. The symptoms of both mitral stenosis[14] and insufficiency[12] have been produced by these tumors, the type apparently depending upon the degree of prolapse of the tumor through the valve. An atrial tumor arising near the mitral orifice and overlying the opening may produce a stenotic effect, whereas a tumor arising in the same area which is pedunculated may prolapse into the ventricle resulting in stenosis or, by preventing apposition of the leaflets, lead to insufficiency. That a similar obstructive mechanism may prevail when the tumor arises in the right atrium is demonstrated by the 2 patients with myxomas to be described. In these patients, a stenotic effect on the tricuspid valve resulted, and, in addition, one of the patients exhibited a right-to-left shunt through an atrial septal defect. Characteristically, the myxomas are whitish,

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From the Division of Thoracic Surgery, Henry Ford Hospital, Detroit, Mich.

Read at the Fortieth Annual Meeting of The American Association for Thoracic Surgery at Miami Beach, Fla., May 11-13, 1960.

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Aortography (slide) demonstrated a single coronary vessel coming off the aorta. The left coronary is not seen.

This slide is the artist's drawing of the conditions exhibited at surgery, showing a large anomalous vessel arising from the pulmonary artery. It was quite feasible to turn down the left subclavian artery and to anastomose it with the distal divided anomalous coronary artery.

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This slide shows a rather good match between the two vessels and the adequate length of the left subclavian artery. Unfortunately, we could not get the child off the bypass.

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DR. RICHARD M. PETERS, Chapel Hill, N. C.—I'd just like to ask Dr. Sabiston one question about this very nice presentation, and that is whether he really thinks the revascularization is the important step, or whether the ligation of the anomalous coronary is really the effective therapy.

DR. SABISTON (Closing).—In answer to Dr. Peters' question concerning the value of the epicardial revascularization procedure, I regard it as being of secondary importance Ligation of the anomalous coronary artery is the definitive part of the operation.

DIAGNOSIS AND SURGICAL TREATMENT OF INTRACARDIAC MYXOMA AND RHABDOMYOMA

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lobulated tumors which arise from a pedicle in the region of the foramen ovale of the atrial septum. Hemorrhage, necrosis, and calcification have commonly been noted within the tumors which are composed of a loose myxomatous connective tissue stroma. Mucin stains, such as mucihematin, are positive. The evidence that they are true neoplasms rather than atypical thrombi is convincing.[13]

Primary rhabdomyoma of the myocardium is a rare cardiac tumor which has heretofore only been reported as a necropsy finding. They are usually part of a generalized hamartomatosis involving the brain, skin, heart, kidneys, and occasionally other abdominal viscera. The cerebral component consists of localized glial proliferations (tuberous sclerosis) and the dermis develops nodular connective tissue overgrowth (adenoma sebaceum). The latter may not appear until late in the course of the disease which is prone to terminate with epilepsy and mental deterioration. Many patients do not live beyond the first year of life. The localized areas of tissue overgrowth are probably best categorized as hamartomas or developmental abnormalities[17] rather than neoplasms. Cardiac rhabdomyomas are most commonly found as multiple small nodules frequently located within the ventricular myocardium,[15, 16, 17] although occasionally larger, solitary tumors have been found. The tumors are unencapsulated and microscopically show "spider cells" which stain for glycogen and occasionally exhibit the cross striations of cardiac muscle. Fibrosis and calcification are frequently present.

Von Recklinghausen is credited by Farber[17] with the original description. The patient we are presenting exhibited the findings of right ventricular outflow tract obstruction similar to infundibular pulmonic stenosis. Diagnosis and surgical treatment of this cardiac tumor have not previously been reported.

CASE REPORTS

CASE 1.*—A 51-year-old housewife was admitted to Henry Ford Hospital on Jan. 23, 1957, with the complaints of dyspnea and drenching night sweats of 3 months' duration. A period of difficulty in controlling movements of the right side of the body had occurred several months and again 3 weeks preceding admission. Positive findings were confined to the heart and consisted of a rough systolic murmur over the xyphoid process. The blood pressure was 110/70 mm. Hg and routine laboratory examinations were normal. The venous pressure and the arm-to-tongue circulation time was normal. The liver edge was palpable below the right costal margin. Another examiner heard an apical systolic murmur. At a subsequent examination a presystolic rumble was audible at the apex, accompanied by a gallop rhythm. A fourth consultant noted distended neck veins at the time of his examination and was unable to detect a murmur. Cyanosis was noted on several occasions. The electrocardiogram demonstrated a changing pattern which initially showed a nodal rhythm with low voltage complexes. The T waves subsequently became inverted, suggesting acute myocarditis and anteroseptal damage. On four later occasions, electrocardiographic tracings were interpreted as normal. Chest roentgenograms and fluoroscopy demonstrated no significant abnormalities. The brachial arterial oxygen saturation, which was 76 per cent while breathing air, rose to 89 per cent on breathing 100 per cent oxygen.

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*This patient has previously been reported by Coates and Drake.[18]

Because of a history of increased dyspnea occasioned by lying on the left side, brachial arterial oxygen samples were drawn with the patient in the left and right lateral decubitus positions. While breathing room air, the sample drawn in the left lateral position was 55 per cent saturated and that drawn in the right lateral position was 69 per cent saturated. Right-sided cardiac catheterization revealed essentially normal pressures at that time and the catheter passed through the atrial septum into the left atrium. A blood sample from the latter location was 89 per cent saturated. Dyspnea, neck vein distension, and cyanosis progressively increased during the next few days. The tentative diagnosis at this point was Ebstein's malformation of the tricuspid valve. Angiocardiography was performed which demonstrated an enlarged right atrium containing a lobulated mass which extended through the tricuspid valve into the right ventricle (Fig. 1).

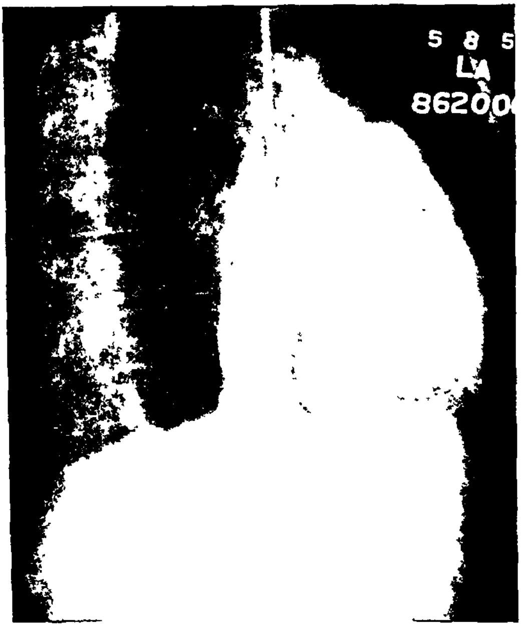


Fig. 1.—Case 1. Angiocardiogram with right ventricular injection. The lobulated filling defect in the right atrium and right ventricle is produced by a myxoma.

Operation.—Right atriotomy was carried out on April 25, 1957, using total cardiopulmonary bypass for a period of 30 min. with the DeWall-Lillehei bubble oxygenator. The perfusion rate was 76 c.c. per kilogram per minute through the left subclavian artery. A transverse thoracotomy in the third intercostal space was utilized. During the venous cannulations which were done through the atrium alongside the tumor, cardiac action deteriorated which necessitated rapid completion and institution of perfusion assistance. The heart was stopped with acetylcholine and right atriotomy performed. The tumor, which protruded into the left atrium through a septum secundum defect and through the tricuspid valve into the right ventricle, was removed along with the site of attachment to the rim of the atrial defect (Fig. 2). The atrial septum with the resulting defect from excision of the pedicle was closed with two rows of 2-0 silk sutures. Cardiac contractions promptly resumed after removal of the aortic clamp and decannulation followed. Marked postoperative improvement was soon noted with clearing of the signs of venous hypertension and return of the arterial oxygen saturation to normal (96 per cent). The patient was discharged on June 16, 1957, and has remained well.

Pathologic Findings.—The tumor was lobulated, glistening white, and, microscopically exhibited the loose myxomatous stroma of a cardiac myxoma (Fig. 3).

CASE 2.—A 54-year-old housewife was first admitted to Henry Ford Hospital June 1, 1959, complaining of frequent headaches and episodes of palpitation of 6 years' duration. Increasing shortness of breath on exertion had been noted during the preceding 9 months and this was accompanied by flushing and excessive perspiration. Periorbital and lower extremity edema were more recent developments. Significant physical findings consisted of a generalized, brown skin pigmentation, fullness of the neck and antethoracic veins, and periorbital edema. The liver was moderately enlarged but did not pulsate. Heart sounds were described as being of tic-tac quality and accompanied by an apical systolic murmur. A mid-diastolic murmur was also heard along the left lower sternal border. Different murmurs were subsequently noted by other examiners. Blood pressure was 120/80 mm. Hg.

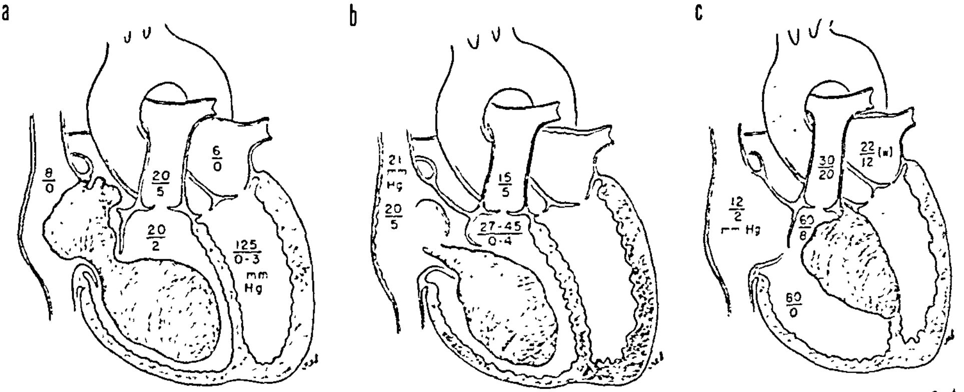


Fig. 2.—*a*, Case 1. Myxoma arising from the right side of an auricular septal defect and projecting into the left atrium and right ventricle. Right heart pressures are not elevated but a right-to-left shunt was demonstrated.

b, Case 2. Right atrial myxoma arising from septum and prolapsing into right ventricle. Elevated right atrial and ventricular pressures are present.

c, Case 3. Ventricular septal rhabdomyoma producing subvalvular pulmonary stenosis. Right ventricular hypertension is present. Mild elevation of the pulmonary artery and wedge pressures was thought to be produced by extension of the rhabdomyoma into the mitral valve area.

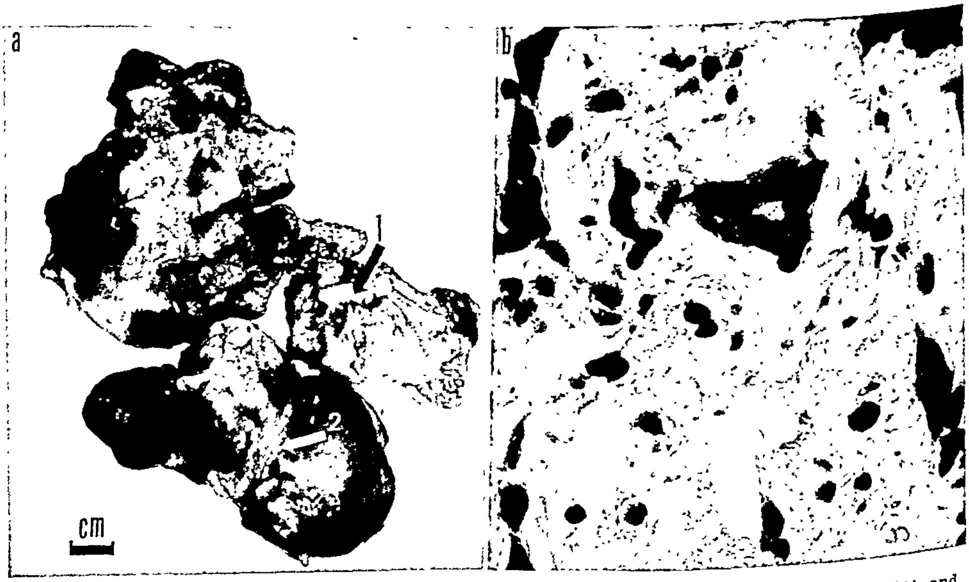


Fig. 3.—*a*, Right atrial myxoma from Case 1 which shows pedicle of origin *(1)* and indentation produced by tricuspid valve *(2)*. *b*, Microscopic appearance of loose myxomatous stroma.

Routine laboratory examinations were normal. Chest roentgenograms and fluoroscopy failed to show significant abnormalities (Fig. 4). A carcinoid syndrome was suspected because of the flushing and perspiration but was not substantiated by laboratory tests. Peaked T waves and right atrial hypertrophy were noted in the electrocardiogram. Peripheral venous pressure was 260 mm. saline and the arm-to-tongue circulation time was 22 seconds. *Right cardiac catheterization* demonstrated normal oxygen determinations. The pressures were found elevated proximal to the pulmonary valve with a right atrial pressure of 20/5 mm. Hg and a superior vena caval mean pressure of 21 mm. Hg. The right ventricular systolic pressures varied between 27 and 45 mm. Hg. Obstruction of the tricuspid valve was indicated by an end diastolic gradient of 15 mm. Hg across the valve. The tentative diagnosis was either tricuspid stenosis or a right atrial tumor. Angiocardiography was advised at this point but the development of multiple venous thromboses in the upper extremities and neck discouraged further venous cannulations. Impaired liver function was indicated by a Bromsulphalein retention of 45 per cent in 15 minutes. The administration of digitalis and diuretics did not lower the venous pressure or subjectively improve the patient. The patient's clinical course rapidly deteriorated and was punctuated by episodes of syncope during which the peripheral pulse disappeared.

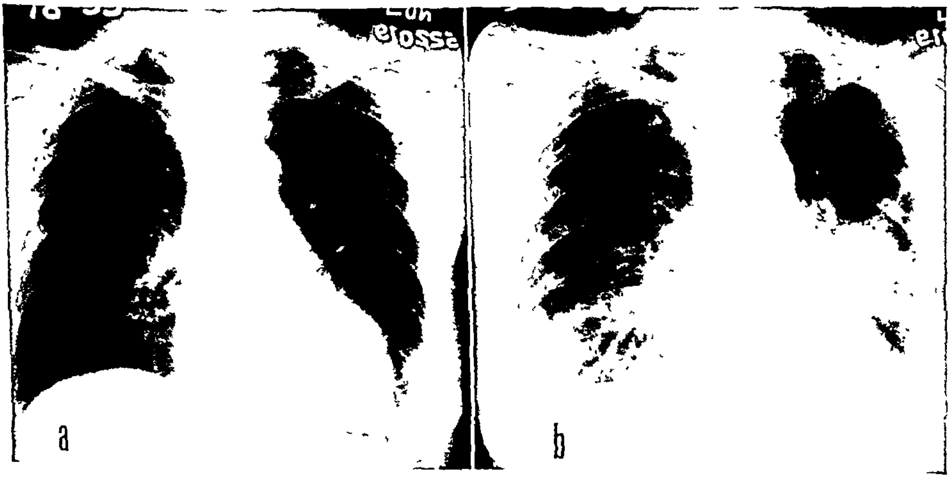


Fig. 4.—Case 2 Preoperative *(a)* and 1 month postoperative *(b)* chest roentgenograms of patient with right atrial myxoma producing obstruction at the tricuspid valve. Specific chamber enlargement is not identified.

Operation.—Operation was carried out on July 21, 1959, using cardiopulmonary bypass of 27 minutes' duration with a bubble oxygenator. A bilateral transverse thoracotomy in the third intercostal space was used. An arterial perfusion rate of 75 c.c. per kilogram per minute was introduced through a femoral cannula. Vena caval cannulations were made through the atrial appendage beside a large intra-atrial mass. The heart was allowed to beat during atriotomy. A portion of the tumor had prolapsed into the right ventricle forming a cast of this chamber (Fig. 2). Manual compression of the ventricle delivered the tumor through the tricuspid valve and into the right atrium from which it was excised along with the area of attachment to the inferior portion of the atrial septum and adjacent inferior vena cava (1.5 by 2 cm.). The septum was repaired, atriotomy closed, and protamine administered prior to decannulation. The facial and lower extremity edema rapidly subsided and the patient was discharged on Aug. 26, 1959. When last seen 6 months postoperatively, she was completely free of symptoms and leading a *normal life.*

Pathologic Findings.—The tumor was friable, lobulated, glistening white, and measured 10 by 8 by 4 cm. (Fig. 5). The microscopic appearance was similar to that found in Case 1. The site of origin from the atrium and vena cava showed superficial attachment with no invasion of the underlying myocardium.

CASE 3.—A 7-year-old boy was admitted to Henry Ford Hospital Oct. 14, 1958, with a history of shortness of breath on exertion. The parents stated that a cardiac murmur had been known to be present since birth. Two unsuccessful attempts to perform cardiac catheterization had previously been made in another city. The child was on a high protein diet because of spontaneous hypoglycemia which had been manifested by occasional loss of consciousness which had required intravenous administration of glucose. Examination revealed a well-developed boy with a mild pectus excavatum. There was a thrill and systolic murmur over the pulmonary artery area. Chest roentgenograms and fluoroscopy demonstrated mild cardiomegaly due to right ventricular enlargement (Fig. 6). The electrocardiogram was interpreted as showing counterclockwise rotation and a bizarre conduction disturbance (Fig. 7). *Cardiac catheterization* was performed through the right saphenous vein on July 15, 1958, by Dr. Edward Green of the Pediatric Cardiology Division. The blood oxygen determinations were normal; however, pressure measurements revealed right ventricular hypertension. During the withdrawal of the catheter from the pulmonary artery where the pressure was 30/20 mm. Hg, the pressure rose to 60/0 mm. Hg high in the right ventricular outflow tract and 80/0 mm. Hg in the low right ventricle (Figs. 2 and 8). The corresponding mean pressures in millimeters of mercury were 20 in the pulmonary artery, 22 high in the outflow tract, and 30 in the low right ventricle. The wedge pressure was 22/12 mm. Hg. The catheter was noted to deviate markedly in the region of the ventricular septum prior to entering the pulmonary artery. These data were interpreted as demonstrating moderate right ventricular outflow tract obstruction and some evidence of

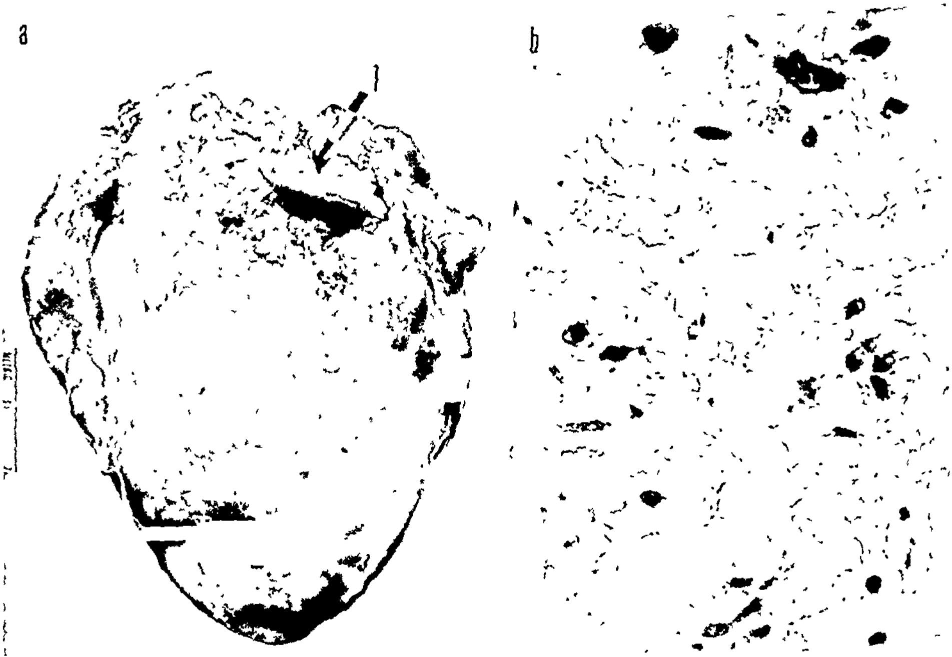


Fig. 5.—Case 2. *a*, Excised right atrial myxoma which had prolapsed into and formed a cast of the right ventricular chamber. Pedicle demonstrated at *1*. *b*, Loose myxomatous stroma which stains for mucin.

obstruction at the mitral valve. Angiocardiography and cinecardiography with right ventricular injection confirmed the presence of a mass partially obstructing the subvalvular pulmonary area (Fig. 9). A rhabdomyoma of the ventricular septum was postulated by Dr. E. Green.

Operation.—On Oct. 14, 1958, cardiopulmonary bypass for a period of 67 minutes was carried out with a bubble oxygenator for resection of the intracardiac tumor. A bilateral, transverse, third interspace incision was used with subclavian artery cannulation.

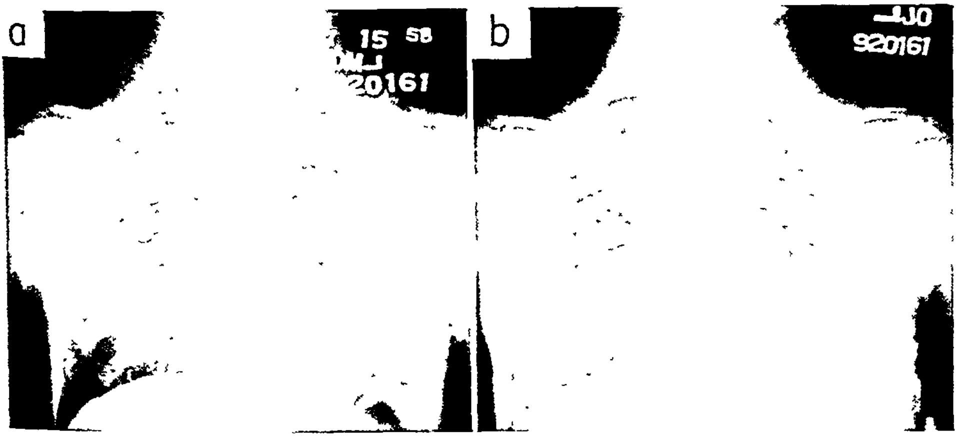


Fig. 6.—Case 3. Preoperative *(a)* and 6 weeks postoperative *(b)* chest roentgenograms of patient with ventricular septal rhabdomyoma which produced subvalvular pulmonic stenosis.

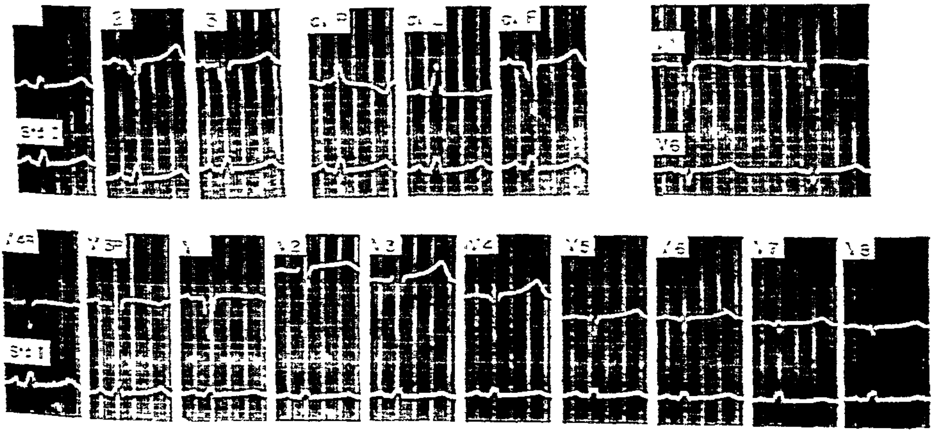


Fig. 7.—Case 3. Preoperative electrocardiogram of patient with cardiac rhabdomyoma which shows normal sinus rhythm. Bizarre ventricular activation is present and probably is due to abnormal intraventricular conduction.

The perfusion rate was 90 c.c. per kilogram per minute. After opening the pericardium, the anterior surface of the heart overlying the ventricular septum was noted to contain a bulging, whitish, firm, noncontractile area which measured 3 by 2 cm. There was a thrill beneath this area which was transmitted into the pulmonary artery. A mass, occupying the septal region, could be vaguely outlined. The heart was stopped with acetylcholine and right ventriculotomy performed. The pulmonary valve was normal; however, the outflow tract was partially obstructed by a mass which arose in the ventricular septum (Fig. 10).

Generous portions of the projecting muscle-like mass were then excised much as might be done with infundibular stenosis. The resection was carried to a depth at which an aspirating needle obtained bright red left ventricular blood after passing a few millimeters farther into the mass. Frozen section examination was said to show muscle. Cardiac action was restored by removing the aortic clamp and the ventriculotomy was repaired. The tumor was not discrete and portions of it could be palpated extending into the atrial septum between the two auriculoventricular valves. Inasmuch as the preoperative studies had demonstrated relatively minor malfunction in the mitral valve region, nothing further was done and decannulation followed. Recovery was complicated by a left chylothorax of 6 days' duration which was treated by tube drainage. Thoracic duct injury apparently resulted from dissection about the left subclavian artery which was used for arterial inflow.

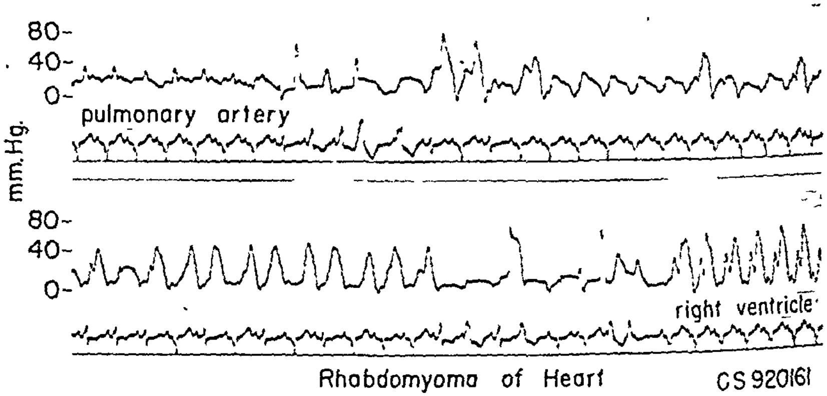


Fig. 8.—Case 3. Pull-through of pulmonary valve and right ventricle during right heart catheterization of patient with ventricular septal rhabdomyoma. An infundibular area of transition between pulmonary artery and right ventricle is demonstrated as well as right ventricular hypertension.

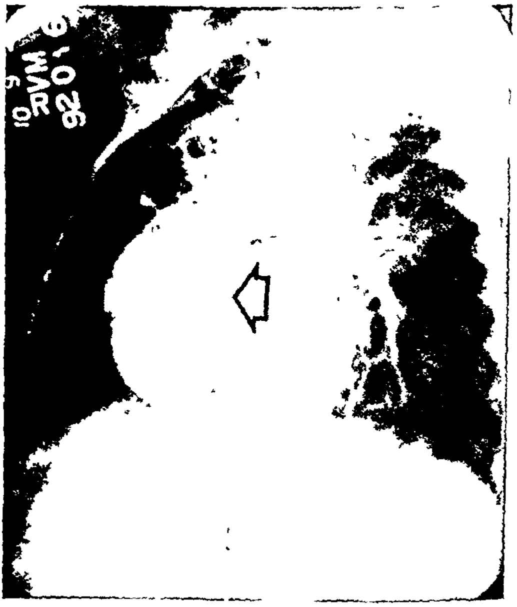


Fig. 9.—Case 3. Angiocardiogram in left, posterior oblique projection with right atrial injection. The septal region of the right ventricular outflow tract is deformed by an irregular filling defect due to the rhabdomyoma.

Pathologic Examination.—Examination of the resected tissue revealed hyaline fibrosis and calcification within a rhabdomyoma (Fig. 11). Foam cells showing a positive stain for glycogen were not well demonstrated. Some relatively normal appearing cardiac muscle was visible. Because of the frequent association of cardiac rhabdomyoma and tuberous sclerosis, investigations were then undertaken to determine the presence of the latter condition.

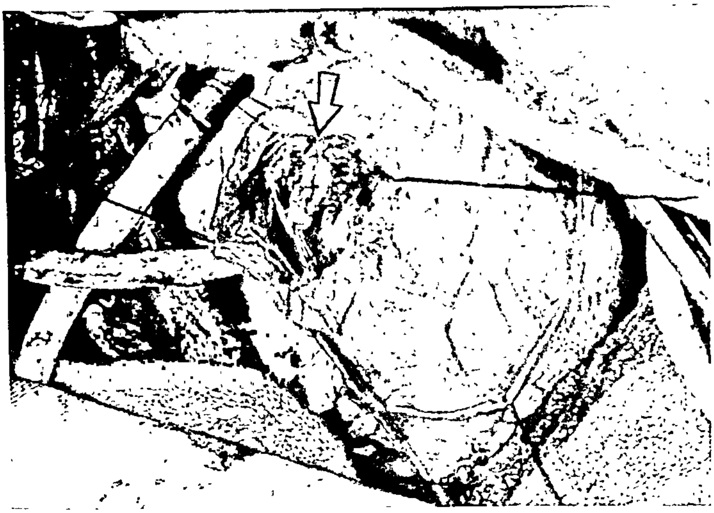


Fig. 10.—Case 3. Right ventriculotomy during cardiopulmonary bypass in patient with ventricular rhabdomyoma. Patient's head is above top of photograph. The bulging ventricular septal mass prior to excision is indicated by *arrow*.

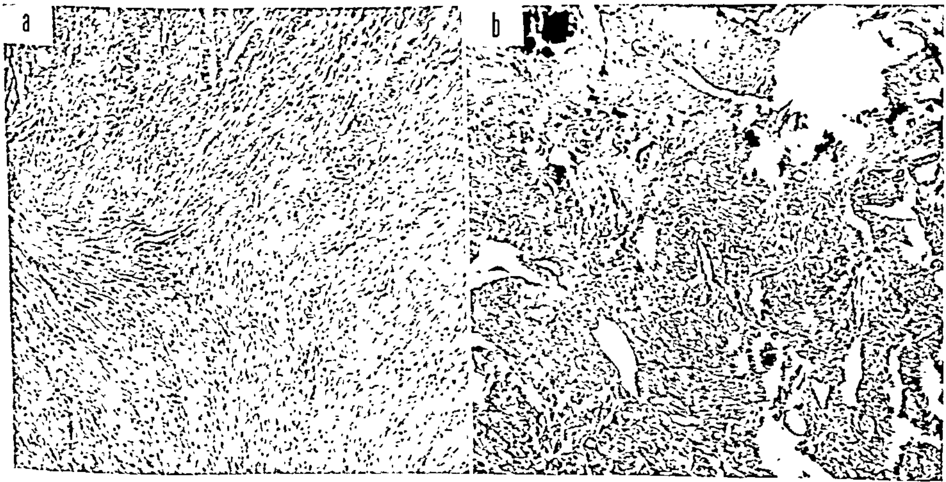


Fig. 11.—Case 3. Normal cardiac muscle *(a)* for comparison with the rhabdomyoma *(b)*. Hyaline fibrosis and calcification are present within the rhabdomyoma.

There was mild mental retardation with an I. Q. of 73. The electroencephalogram suggested left cerebral hemisphere dysfunction. Funduscopic examination revealed a suggestion of the "soapy spots" seen in tuberous sclerosis. The skin nodules of adenoma sebaceum were not present. The child was discharged Nov. 16, 1958. When last seen on April 3, 1960, he had gained weight and was said by the parents to be free of dyspnea on exertion. Periodic runs of premature beats were noted and, for this, daily quinidine was administered. The murmur over the pulmonary artery was faintly audible and no mitral murmur could be heard.

DIAGNOSTIC CONSIDERATIONS

Primary intracardiac tumors may be diagnosed with certainty by angiocardiography, therefore consideration of the possibility becomes the most important aspect of diagnosis when evaluating a cardiac patient. Since essentially all myxomas arise from the auricular septum, these tumors can be expected to produce disturbance of cardiac function primarily at the atrioventricular valves.

Left Atrial Myxoma.—Three quarters of the reported myxomas arose in this location and produced obstruction of the mitral valve or occasionally insufficiency. As further evidence of the similarity to rheumatic mitral stenosis, 9 of 14 patients operated upon with tumors in the left atrium had the lesion first demonstrated at the time of exploration for an intended closed mitral commissurotomy. Retrospectively, certain aspects of these cases suggest atypical or unusual features. The absence of a rheumatic fever history may be of some help, however, a significant number of patients with bona fide rheumatic mitral stenosis do not recall this event. A hint may also be gained from the ascultatory findings if the location, intensity, or character of the murmur are noted to change. While disappearance of the murmur in certain positions may be helpful, the opposite finding, accentuation of the murmur, would not be of assistance in the case of diastolic murmur as this too is a characteristic of rheumatic mitral valve disease. The opening snap and accentuated first heart sound of mitral stenosis have been recorded with the phonocardiogram in a case of left atrial tumor.[19] Mitral insufficiency findings are apparently much less common than those of stenosis; however, one recorded case of left atrial tumor was first diagnosed at the time of open-heart surgery for repair of mitral insufficiency.[12]

The clinical course and response to treatment have been a somewhat more reliable indication that the patient with mitral valve findings may have something other than a scarred rheumatic valve. A history of arterial embolization in the absence of significant cardiac findings may suggest left atrial tumor. Four of the 14 patients previously operated upon with tumors in this location had such a history. Paradoxical arterial embolization occurred through an atrial septal defect in our Case 1. Movement of the tumor, presumably produced by change in body position, may account for the observation that these patients often prefer to lie in certain positions or note aggravation of symptoms in other positions. This characteristic is frequently mentioned in the cases previously reported of left atrial tumor and should arouse curiosity when noted. Another characteristic which has been commonly recorded is that of poor or no response to adequate therapy for congestive heart failure. Chest roentgenograms and fluoroscopy have been of minor assistance in establishing the diagnosis, except in the case of unusual patterns of atrial calcification. Mild left atrial and right ventricular enlargement have been reported. Although right- or left-sided cardiac catheterization can be expected to reveal findings which support a diagnosis of mitral valve disease, a positive diagnosis can only result when the decision is made to employ radiopaque media.

Right Atrial Myoxoma.—The most frequent hemodynamic change produced by tumors in this location has been obstruction at the tricuspid valve. Although rheumatic tricuspid stenosis occurs rarely as an isolated lesion, these neoplasms are more likely to be confused with intractable congestive failure due to arteriosclerotic heart disease, constrictive pericarditis, or Ebstein's malformation of the tricuspid valve. Case 2 illustrated the findings of tricuspid stenosis as manifested by high peripheral venous pressure with periorbital and ankle edema, and hepatomegaly. Excessive sweating and flushing were noted by both of our patients. Changing murmurs which occasionally disappeared were also recorded in both instances. Positional aggravation of symptoms was noted in Case 1 and confirmed by the finding of greater desaturation of the arterial blood when a specimen was collected in the lateral position as compared to one drawn in the supine position. The right-to-left shunt in this instance occurred through an atrial septal defect. Radiographic examination demonstrated some enlargement of the right atrium in both cases and the electrocardiogram indicated right atrial hypertrophy. A changing electrocardiogram may be seen as demonstrated by one of our patients. Calcification was not visible in either of our patients. At this point, right-sided cardiac catheterization should be considered and a suspicion of tricuspid valve obstruction will be confirmed by finding high right atrial and normal, or near normal, right ventricular pressures. Although Case 1 did not show an elevated right atrial pressure at the time of catheterization, increased peripheral venous pressure was noted clinically on other occasions. Changing right ventricular pressures with systolic variations of as much as 20 mm. Hg were noted during catheterization of both patients. This finding was attributed in hindsight to the changing position of the portion of the tumor which had prolapsed through the tricuspid valve. The absence of a pressure change during a pull-through of the tricuspid area in Case 1 suggested Ebstein's malformation of this valve. Angiocardiography was employed at this juncture in the management of Case 1 and dispelled the confusion which had existed up to this point. A large lobulated filling defect of the right atrial chamber was clearly outlined.

Rhabdomyoma.—Several types of primary cardiac tumors of muscle origin have been found at autopsy. Primary sarcoma and rhabdomyosarcoma have usually occurred as diffusely infiltrating neoplasms which produced death by pericardial tamponade or cardiac rupture.[16, 20] These tumors exhibit metastasis to mediastinal lymph nodes and abdominal viscera. Primary rhabdomyoma of the myocardium, however, is generally considered to be a developmental abnormality or hamartoma and has not been reported as a precursor of the malignant sarcomatous lesions. In a series of 49 necropsies on patients with primary cardiac rhabdomyomas, 8 were large solitary ventricular tumors and the remainder presented as multiple, small tumors throughout the ventricular and auricular myocardium.[17] The multiple small tumors were incidental findings in infants who died from noncardiac causes as contrasted to the larger solitary tumors which were discovered in patients dying with cardiac symptoms. We have recently seen in an 8-month-old infant a mitral valve obstruction which was found at necropsy to be produced by pedunculated rhabdomyoma of the left atrium. Small intramural tumors were also present within the ventricular myocardium. Twenty-four of the 28 cases in the previously mentioned series of 49 autopsies, in which intracranial examination was done, exhibited tuberous sclerosis.

The diagnosis of rhabdomyoma in our patients was based on the angiocardiographic findings. The obstruction was seen to be produced by a mass projecting from the interventricular septum and the configuration could be differentiated from the more nearly concentric type of narrowing seen in infundibular stenosis. The catheterization pressure measurements indicated obstruction of the right ventricular outflow tract below the pulmonary valve. An "infundibular type" pull-through tracing was obtained. Mild right ventricular enlargement was noted on the chest roentgenograms. The electrocardiogram exhibited bizarre conduction disturbances indicating disease of the septal area. A search for the lesions which frequently accompany rhabdomyoma of the heart was partially rewarding in that highly suggestive evidence of tuberous sclerosis was found although adenoma sebaceum was not present.

SURGICAL CONSIDERATIONS

Atrial Myxoma.—Six of the 11 patients having had previously successful resections were operated upon with the use of extracorporeal circulation and 5 with hypothermia. If a myxoma is found at the time of exploration for a planned conventional mitral commissurotomy, as was the case in the majority of left atrial tumors, a decision must be made whether to proceed with removal under hypothermia induced at that time or to excise the tumor at a subsequent operation with the aid of a pump-oxygenator. The patient's condition permitting, our choice would be to use extracorporeal circulation. This method comfortably permitted the 30 minutes of intra-auricular operating time required by each of the 2 reported cases. In both instances more operating time within the heart was necessary than the brief period required to remove the tumor. In Case 1, repair of the atrial septum and, in Case 2, repair of the septum and adjacent inferior vena cava were necessary after excision of the attachment sites. Excellent operative exposure in both cases resulted from the use of a bilateral transverse thoracotomy in the third intercostal space. The supine position is to be recommended as it avoids turning the patient which has produced fatal valve occlusion on the operating table in at least one instance.[21] Cannulation has been readily performed by inserting the catheters through the auricular appendage and passing them alongside the tumor and into the venae cavae. Since nearly all myxomas arise from the vicinity of the foramen ovale, the site of the origin can be sought for in this area and a button of atrial septal wall excised with the tumor. Pathologic examination of this site has shown a superficial attachment without invasion of underlying myocardium. Precautions to avoid air embolism during cardiotomy consisted of rotating the operating table so as to place the atrial opening uppermost and filling the chambers with blood or saline before closure. The ascending aorta was cross-clamped and the heart stopped in Case 1 to produce a dry heart and for prevention of systemic tumor embolization. One reported patient has died as a result of extensive arterial tumor embolization.[22]

Rhabdomyoma.—Cannulation and perfusion for resection of the obstructing rhabdomyoma tissue in Case 3 did not require special considerations. Adequate decompression of the outflow tract resulted from excision of abnormal tissue so that a "patch" in this area was not necessary. If the popular pathologic concept of this lesion holds, namely that the tumor is a developmental abnormality or hamartoma, surgical treatment probably need only consist of excision of obstructing tissue rather than resection of the entire tumor. The latter would not have been consistent with survival in our patient because of the extent and location of the tumor. There is evidence to indicate that a rhabdomyoma may undergo involution, as represented by the findings of fibrosis and calcification in some of the necropsy cases[23] as well as in our patient. The over-all result in our patient may more likely be dependent upon the progression of the tuberous sclerosis which is believed to be present, rather than the cardiac aspects of the case.

SUMMARY

1. Primary cardiac tumors were considered a pathologic curiosity until the development of open-heart surgical techniques. The most frequently encountered tumor is the myxoma which arises in approximately three fourths of the cases from the left side of the atrial septum. Symptoms and findings of mitral stenosis or insufficiency may be produced by a left-sided tumor and closely resemble those of rheumatic valvular disease. Changing murmurs, positional aggravation of symptoms, refractory heart failure, and history of arterial embolization in the presence of minor cardiac findings are clinical features which may assist in the differentiation. Chest roentgenograms, the electrocardiogram, and cardiac catheterization support a diagnosis of disease at the mitral valve but positive identification depends upon angiocardiography.

2. Right-sided atrial myxoma is most likely to be confused with lesions producing a high right atrial pressure, such as rheumatic tricuspid stenosis, intractable arteriosclerotic heart failure, constrictive pericarditis, or Ebstein's malformation of the tricuspid valve. Here again, positive diagnosis depends upon use of angiocardiography. Two patients are presented who had successful removal of right atrial myxomas using cardiopulmonary bypass. One patient demonstrated a right-to-left shunt preoperatively which was most pronounced in the left lateral position. Shunting occurred through an interatrial septal defect. Approximately 30 minutes of extracorporeal perfusion were required in both cases to remove the tumor, excise the site of septal attachment, and repair the resulting defect. The myxoma characteristically has a superficial attachment without invasion of the underlying myocardium and most likely is a neoplasm rather than a thrombus.

3. Primary rhabdomyoma of the heart has heretofore been described as a rare incidental necropsy finding in infants. The tumors are unencapsulated and may be multiple or solitary. They have been found in association with tuberous sclerosis, adenoma sebaceum, and visceral hamartomas and are regarded as a developmental abnormality rather than a true neoplasm. A case is reported in which a ventricular septal rhabdomyoma produced outflow tract obstruction in the right ventricle. The obstructing portion of the tumor was successfully excised during cardiopulmonary bypass. The patient, a child 7 years of age, exhibited some of the signs of tuberous sclerosis. Preoperative diagnosis and surgical treatment of primary cardiac rhabdomyoma have not previously been reported.

ADDENDUM

Since submission of this manuscript, a report of four additional excisions of myxomas with three successes has been brought to our attention. Two of these tumors arose in the left atrium and one in the right atrium. (*Cooley, D. A., Morris, G. C., and Safuh, A.:* Cardiac Myxoma. Surgical Treatment in Four Cases, A. M. A. Arch. Surg. 78: 410, 1959.)

REFERENCES

1. Crafoord, C.: Panel Discussion on Late Results in Mitral Commissurotomy, Henry Ford Hospital International Symposium on Cardiovascular Surgery, Philadelphia, 1955, W. B. Saunders Company.
2. Steinberg, I., Dotter, C. T., and Glenn, F.: Myxoma of Heart: Roentgen Diagnosis During Life in Three Cases, Dis. Chest 24: 509, 1953.
3. Bahnson, H., and Newnam, E. V.: Diagnosis and Surgical Removal of Intracavitary Myxoma of Right Atrium, Bull. Johns Hopkins Hosp. 93: 150, 1953.
4. Bigelow, W. G., Dolan, F. G., and Campbell, F. W.: Effect of Hypothermia on Risk of Surgery, Proc. Soc. Internat. de Chir., 16th Congress, pp. 631, 1955.
5. Scannell, J. G., Brewster, W. R. Jr., and Bland, E. F.: Successful Removal of Myxoma From Left Atrium, New England J. Med. 254: 601, 1956.
6. Bahnson, H., Spencer, F. C., and Andrus, E. C.: Diagnosis and Treatment of Intracavitary Myxoma of the Heart, Ann. Surg. 145: 915, 1957.
7. Hopkins, W. A., and Davis, M. B., Jr.: A. M. A. Medical News 2: 23, 1956.
8. Robertson, R.: Primary Cardiac Tumors: Surgical Treatment, Am. J. Surg. 94: 183, 1957.
9. Chin, E. F., and Ross, D. N.: Myxoma of Left Atrium: Successful Surgical Removal Under Hypothermia, Brit. M. J. 1: 1447, 1957.
10. Ellis, F. H., Jr.: Myxoma of Atrium: Successful Surgical Treatment in Two Cases, M. Clin. North America 42: 1087, 1958.
11. Deshmukh, M., Nichols, H., and Goldberg, H.: Myxoma of the Left Atrium Simulating Restenosis of the Mitral Valve, Am. Heart J. 58: 623, 1959.
12. Wittenstein, G. J., Grow, J. B., and Hoffman, M. S.: Myxoma of the Left Atrium Simulating Pure Mitral Insufficiency: Report of a Case With Successful Removal, Surgery 45: 981, 1959.
13. Prichard, R. W.: Tumors of the Heart, Review of the Subject and Report of One Hundred and Fifty Cases, A. M. A. Arch. Path. 51: 98, 1951.
14. Horlick, L., and Merriman, J. E.: Myxoma of Left Atrium Simulating Mitral Stenosis With Cerebral Emboli, Canad. M. A. J. 77: 582, 1957.
15. Brown, G., and Gray, J.: A Case of Congenital Rhabdomyoma of the Heart, Lancet 1: 915, 1930.
16. Lisa, J. R., Hirschhorn, L., and Hart, C. A.: Tumors of the Heart: Report of Four Cases and Review of Literature, Arch. Int. Med. 67: 91, 1941.
17. Farber, S.: Congenital Rhabdomyoma of the Heart, Am. J. Path. 7: 105, 1931.
18. Coates, E. O., and Drake, E. H.: Myxoma of the Right Atrium, With Variable Right-to-Left Shunt, New England J. Med. 259: 165, 1958.
19. Lefcoe, N. M., Brien, F. S., and Manning, G. W.: An Opening Snap Recorded in a Case of Tumor of Left Atrium, New England J. Med. 257: 178, 1957.

20. Reeves, J. M., and Michael, P.: Primary Tumor of the Heart, Am. Heart J. 11: 233, 1936.
21. Thompson, C. E., and Malhas Z. A.: Myxoma of Left Atrium Simulating Mitral Stenosis, A. M. A. Arch. Int. Med. 95: 614, 1955.
22. Harvey, J. C.: Myxoma of Left Auricle, Ann. Int. Med. 47: 1067, 1957.
23. Landing, B. H., and Farber, S.: Tumors of the Cardiovascular System, Fasicle 7, Armed Forces Institute of Pathology, Washington, D. C., 1956.

DISCUSSION

DR. DWIGHT E. HARKEN, Boston, Mass.—I should like to make four comments based on this interesting discussion of Dr. Taber and Dr. Lam.

The first point is statistical and prompted by experience with our seven intracardiac tumors. Three patients were encountered before open surgery was available. All are dead. Four were encountered with open surgery available, and all are alive, presumably cured. Statistics about cardiac tumors are difficult to remember but by putting handles on them it may help you as it helps me. At autopsy, in generalized carcinomatosis, there is a 2 per cent cardiac involvement. This is often extracardiac. Of so-called intracardiac tumors, 75 per cent prove to be thrombi. Seventy-five per cent of true intracardiac neoplasms are myxomata. Seventy-five per cent of myxomata are in the left auricle.

This leads me to the second point; namely, if we have a lesion commonly located in the left auricle, and most of our reported clinical cases are on the right side, we are obviously missing most of them. The dominant location of these tumors found in the autopsy room, versus the clinical experience, makes this clear, so our index of suspicion and diagnosis must be higher.

This stimulus to suspicion may stem from intermittent symptoms, postural symptoms, intermittent murmurs, persistent low grade fever, or multiple emboli. Of course emboli that on removal show myxoma constitute the absolute diagnosis. Angiocardiography may also be very helpful when one is suspicious.

Furthermore, if our colleagues in the catheter laboratories are alert to the possibility of tumor, particularly now that they are using transseptal catheterization techniques, we will suspect more of these tumors. At catheterization, as the septal needle is passed, no auricular tracings can be obtained. This makes one think of tumor. In fact, two of ours have been so suspected recently.

The third point I want to make is technical. Most of these tumors are in the left auricle and they arise from the fibrous septum. We know where they are and how to get at them. The simple way is through a right thoracotomy and the right auricle. The septum is incised and the pedicle visualized. It can then be picked up very much as one picks up the stem of a bunch of grapes.

By excision of the base of the stem, in fact the pedicle, we can lift out the tumor much more simply than if we go in through the left side. We must remember that we are going for game; that this operation is for cure. Therefore this invasive tumor can be cured only by wide excision of the base and then repair of the septal defect that we have created.

The fourth point concerns policy. If we discover a tumor in the course of exploration for mitral stenosis, we should withdraw for a later open-surgical extirpation. In closing the left auricle after the exploration, great care must be exercised to avoid reducing the size of the chamber of the auricle. Even tying off the base of the appendage may compromise the size of the auricle enough to cause prolapse of the tumor into the mitral orifice.

Finally, familiarity breeds success, and Dr. Lam and Dr. Taber have increased our familiarity with tumors of the heart.

DR. BENSON B. ROE, San Francisco, Calif.—Dr. Taber is to be congratulated for a valuable contribution to this interesting subject which has now grown in importance and in experience. I imagine the combined experience in this room would now probably amount to well over 100 cases, since we are more familiar with open-heart techniques.

I would agree that the use of the pump oxygenator under direct vision is the route of choice for dealing with these lesions, but it does not always provide all the answers, and it is not always immediately available in acute situations Two of our patients in recent experience illustrate these points quite dramatically

(Slide) This tumor was discovered in a middle aged woman during exploration for supposed mitral stenosis, and, as you can see from the size of the lesion, it was too large to remove through the atrial appendage. It was my intention to withdraw and reapproach this patient under direct vision, but the general exploration caused it to become dislodged and free floating in the auricle. Therefore, every time the finger was withdrawn, total occlusion occurred We were faced with the proposition of letting her die from the occlusion or of exsanguinating in the attempt to remove it

We chose the latter course, and the patient developed ventricular fibrillation This is what saved her, because the exsanguination was not complete; the arrested circulation permitted us to close the atrial tear, to institute cardiac massage, to replace the blood loss, and to defibrillate the heart. The patient went home in 8 days after an uneventful recovery (Laughter)

The second patient was a small child with an iliac embolus from a tumor, and the diagnosis was made histologically from the extracted embolus Armed with our experience in the first case, we approached the lesion under direct vision, having deliberately induced ventricular fibrillation before opening the left atrium. We were delighted to have done so, because we encountered a large tumor which occupied nearly the entire atrial cavity and which had the consistency and friability of jellied consomme Thus, we would have induced further and probably fatal emboli, had the heart not been inactive.

The purpose of my discussion is to suggest the necessity of having available, in the operating room, methods of inducing ventricular fibrillation in unpredictable circumstances, such as the encountering of clots or tumors which may embolize

DR EARLE B MAHONEY, Rochester, N Y —I rise not to present our 2 cases but to show you, if the projection will work satisfactorily, the angiocardiogram on 1 of the cases This patient had a right atrial myxoma, which presented as tricuspid stenosis, and we think that seeing this pedunculated tumor during angiocardiography presents a vivid picture of the pathophysiology

(A moving picture was shown)

I think you can see in this particular patient that the tumor is prolapsing through the tricuspid valve and extending up into the outflow tract of the right ventricle This was a very large tumor, which was primarily in the ventricle, extending down into it by way of its pedicle, as was shown by Dr Taber

The second was attached by a very short pedicle to the region of the foramen ovale, and this one is swinging just like a pendulum, first through the atrium, through the tricuspid valve, and into the ventricle, back and forth with each cardiac cycle

DR EGBERT H FELL, Chicago, Ill —Dr. Lam said some time ago when he asked me to discuss this paper that he hoped it would flush out the experiences that the members of this Society have had with intracardiac tumors I believe he and his associates are accomplishing their objective

I had the privilege in July, 1954, of seeing Professor Crafoord's patient from whom, I believe, the first successful intracardiac tumor was removed from the left atrium He and Dr Senning are to be commended for this achievement

We have had 2 patients with intracardiac tumors and they have taught us two important facts. (1) If one explores and finds an intracardiac tumor, it should be removed as soon as possible with the aid of extracorporeal circulation 2 Tumors in the left atrium are satisfactorily and, we believe, more easily removed through the right atrium

This slide shows a large pedunculated tumor, much like the one shown by Dr Mahoney, but it contained considerable calcium, thus, an angiocardiogram was not necessary The fluoroscopic examination revealed the tumor moving with the blood flow, and it appeared to be attached to the lateral wall of the right atrium This was before the days of the pump oxygenator and we attempted to remove it with the aid of hypothermia. We did not because the heart went into ventricular fibrillation, resulting in great difficulty in restoring normal function.

Six months later when we attempted again to remove the tumor we found soft granulation tissue had covered the previously smooth surface. Exploration and manipulation of the tumor caused the soft granulations to break off, resulting in multiple pulmonary emboli and death. The next two slides show the gross appearance of the tumor with its granulations and the photomicrograph that is diagnostic of a rhabdomyoma. Some pathologists believe that this tumor is caused by a glycogen storage disease.

This slide shows a pedunculated myxofibroma much like the one discussed by Dr. Taber and Dr. Lam. It was removed a year ago and we first found it at exploration of the left atrium, believing the patient had mitral stenosis. As I was putting my finger in the left atrium my intern asked, "Have you ever felt a ball-valve tumor?" I replied, "I'm feeling one now." Two weeks later the tumor was successfully removed through the right atrium. The atrial septum, at the level of the foramen ovale, the site at which the tumor was attached, was excised, this large tumor was delivered, and the septum was then repaired. This microscopic slide revealed this tumor to be a myxofibroma.

We believe, with the aid of the heart-lung machine, tumors in either atrium are best and more safely removed from the right side.

DR. CLARENCE CRAFOORD, Stockholm, Sweden.—My thanks to you, our President, for calling on me, and to Dr. Taber for mentioning my name in connection with this matter.

I just want to raise one point in connection with Dr. Harken's discussion. I think it is not wise—I would warn—for the transseptal or direct puncture and catheterization of the left auricle, because these tumors are very friable, and catheterization of the left atrium might give rise directly to embolization.

I think, if it is necessary for a diagnosis to make an angiocardiogram that it is best made selectively from the pulmonary artery, as we did in our case.

Dr. JOHN Y. TEMPLETON, III, Philadelphia, Pa.—I wish to present another case of a right atrial lesion which we thought was somewhat unusual. It occurred in a 37-year-old woman who had had a hysterectomy for a fibroid tumor several months before, at which time her heart was quite normal. Subsequently she developed episodes of syncope and very bizarre changing heart murmurs. This led the clinicians to suspect an intracardiac tumor, and this is shown in the right atrium on the first slide.

(Slide) I think the filling defect which one sees here lying in the right atrium is quite evident.

Further investigation disclosed that she had a severe thrombocytopenia, and efforts were made to improve this with corticoids, etc. During this period of therapy she developed a left lower lobe infarction. She failed to respond from the standpoint of her thrombocytopenia, and splenectomy was done. Her infarction cleared to some extent, and the sputum diminished.

She was operated upon with the purpose of removing this right atrial myxoma. We found that there was the knob-like projection that one sees on the angiocardiogram, but this arose from a solid mass extending upward from the vena cava. We found a lesion in the aorta which looked quite similar to that which Dr. Longmire has described.

(Slide) This mass was divided below the renal veins and the distal portion removed by virtue of a great deal of traction. One can see that this portion is intact on this side. On this side, however (indicating), it is obvious that fragments of clot have been left behind.

Having removed the lower part, we then returned to the atrium and easily removed the part that was there. The mass appeared intact except for this distal portion which I showed earlier.

This slide demonstrates the extent of the lesion. One observes this knob-like projection lying up in the atrium, and the extension well down below the inguinal ligament on one side.

Unfortunately, although the patient's immediate postoperative condition was quite satisfactory, she died in right ventricular failure. Autopsy examination disclosed a great deal more of this process which involved the pulmonary arterial system on both sides. It was to this further extension, more than we have shown here, that her death was attributed.

The pathologists have diagnosed this as an organized thrombus, and it is probable that this is where her platelets went.

DR. TABER (Closing).—To confuse the issue even further, here is a slide showing a pedunculated rhabdomyoma which, prior to seeing Dr. Fell's case, I didn't realize could be quite so polypoid. This was one in an 8-week-old child who died following catheterization.

I would like to thank Drs. Harken, Roe, and Mahoney for their eloquent emphasis of the points involved in these problems. Probably the biggest problem confronting the surgeon is the decision which he has to make when confronted by this tumor at the time of mitral commissurotomy. Three fourths of them have been diagnosed in this manner.

We would like to use an open operation, if possible. If a tragedy happens, such as the breaking off of this tumor, as Dr. Roe demonstrated, obviously the thing is going to have to be removed at that time.

The other point that I might mention is in regard to diagnosis—it seems to me this is the area in which we need to improve our management of cardiac tumors. The surgical techniques are available, if we can just diagnose them properly.

Angiocardiography should certainly show lesions on either side. Certainly, if suspected, it is something that can be picked up in this manner. I think it is similar to the situation that exists with other uncommon cardiac lesions—for instance, constrictive pericarditis—which is usually called something else before the surgeon sees the patient; and therefore, we have to be cognizant of this lesion in evaluating this kind of patient.

VASOMOTOR REGULATION DURING EXTRACORPOREAL CIRCULATION AND OPEN-HEART SURGERY

Paul W. Sanger, M.D., Francis Robicsek, M.D. (by invitation),
Frederick H. Taylor, M.D., Terry T. Rees, M.D. (by invitation),
and Robert E. Stam, M.D. (by invitation), Charlotte, N. C.

There have been scattered observations published in recent literature regarding extracorporeal circulation which indicate that the importance of the vasomotor tone is being recognized. Galetti and associates[8] described "spontaneous" shifts in the blood volume between the patient and the oxygenator. Similar observations were made by Waldhausen and associates[23] who found this "wandering of blood volume between the patient and oxygenator" a constant phenomenon. Blair and associates[2] studied experimentally the effects of temporary total circulatory occlusion, and found that the reduction of blood flow through the arterial system resulted in dramatic increase of the vasomotor tone. They also found that the release of this occlusion resulted in a high degree of "overshot" in the arterial pressure, which was taken as an index of vasomotor activity. This response was completely eliminated if the body temperature was reduced below 28° C.

A very common but interesting observation was that despite a flow rate equal to the calculated normal cardiac output, the arterial pressure was usually subnormal during perfusion.[4, 13, 15, 16, 17, 22] Merendino,[15] realizing the significance of vasomotor regulation in the distribution of blood flow, advocated the use of vasopressor agents in patients with systemic hypertension who were undergoing open-heart surgery ". . . in view of difficulty in obtaining near-normal perfusion pressures." Andersen and Senning[1] found the vascular system reacting strongly to vasoconstrictors during perfusion and expressed their opinion that the body's natural vasoregulation plays a dominant role in the magnitude and redistribution of blood flow. Boyd[3] described immediate decrease of the cardiac output soon after cardiopulmonary bypass.

Another common observation during total body perfusion was that, despite constant perfusion rates, the perfusion pressure varied considerably. If effort was taken to keep these pressures at a steady level, the flow rate had to be readjusted repeatedly. This indicated significant alteration in the physiologic condition of the vascular system of the perfused individual.

This work was done at the Department of Thoracic Surgery, Charlotte Memorial and Mercy Hospitals, and at the Heineman Laboratory for Cardio-Pulmonary Research Charlotte, N. C.

Supported by grants from the John A. Hartford Foundation and the United Medical Research Foundation of North Carolina.

The purpose of our study is to describe some of these changes and discuss their possible clinical significance.

MATERIALS AND METHODS

A. *Clinical.*—

In an 8-month period, hemodynamic observations were made during total body perfusion on 42 patients who underwent open-heart surgery at Charlotte Memorial and Mercy Hospitals. These patients were divided into categories with relation to clinical diagnosis (Table I).

TABLE I

Atrial septal defect (secundum type)	9
Atrial septal defect (complicated)	6
Ventricular septal defect	17
Tetralogy of Fallot	7
Others	3
Total	42

One hour before surgery the patients were medicated with intramuscular injections of Demarol, Thorazine, and Chlor-Trimeton. Anesthesia was induced with intravenous Pentothal sodium and maintained with a mixture of Fluothane and oxygen. Small doses of succinylcholine were administered as required.

The right anterolateral approach was used in uncomplicated atrial septal defects; in other cases the heart was exposed through an anterior longitudinal mediastinotomy. The right femoral vessels were cannulized for arterial return and for the drainage of the inferior caval system. The upper venous drainage was accomplished by a catheter inserted via the right auricular appendage into the superior vena cava.

All blood from the venae cavae was drained via a 45 cm. siphonage into the extracorporeal circuit, which consisted of a venous reservoir, bubble-trap, twin De Bakey rotor-pumps, rotating oxygenator, and a filter. The blood aspirated from the open heart was delivered into a sedimentation reservoir and returned when necessary. The blood in the extracorporeal circuit was kept at normal body temperatures by an infrared heating system. During the bypass, a gas mixture of 97.5 per cent oxygen and 2.5 per cent carbon dioxide was introduced into the free-exhaust oxygenator cylinder with a flow rate of 10 L. per minute.

To re-check the performance of the heart-lung machine and to decompress the pulmonary circuit, total body perfusion was started 1 minute before cardiotomy. Blood flow rates, ranging from 70 to 100 c.c. per minute per kilogram of body weight were used for smaller children, decreasing to 50 c.c. for adults. In selected cases, cardiac arrest was introduced using a mixture of potassium chloride, magnesium sulfate, and Prostigmin. Extracorporeal circulation was sustained until the cardiotomy incision was completely closed and the heart was beating forcefully.

Regarding principles of operative indication and surgical management, as well as details of the perfusion technique, these were reported in our works published previously on this subject.[20, 21]

The extracorporeal circuit described was tested experimentally and clinically. Our data were in accordance with that of others,[9, 11, 14, 22] who indicated it is highly efficient in gas-exchange and pumping efficiency. The arterial line oxygen saturation was an average of 96 per cent and we did not find evidence of significant acid-base imbalance or hemolysis during perfusion. Eighty-four open-heart operations were performed on human beings with the rotating disc oxygenator in our institute with an operative mortality rate of 10.5 per cent. In no case was death due to insufficiency or mechanical failure of the pump-oxygenator. For this reason we abandoned continuous monitoring of blood gases or blood pH during open-heart surgery.

The temperature of the blood was measured with a thermotransister built into the "arterial" end of the oxygenator. The revolution/minute ratio of the rotor pumps and the rotating discs was indicated on tachometers. Continuous electrocardiograms were recorded.

The central venous and aortic pressures were measured by polyethylene catheters inserted through the left femoral vessels. These catheters were connected to strain gauge manometers and a multichannel oscillograph. The venous discharge into the machine and the arterial return to the patient were measured and recorded by specially designed flowmeters.[18, 19]

The total systemic circulatory resistance was calculated using the formula:

$$R = \frac{P_{am} - P_{vm}}{\left(\frac{F}{60}\right)} \bullet 1332$$

in which

R = systemic circulatory resistance (dyn. sec. cm.$^{-5}$)
P_{am} = mean aortic pressure (mm. Hg)
P_{vm} = mean central venous pressure (mm. Hg)
F = systemic blood flow (c.c./min.).

B. *Experimental.*—

To obtain observations "undisturbed" by the cardiac anomaly and by the heart operation itself, a series of perfusions was performed on dogs.

Healthy mongrel dogs of both sexes, weighing from 12 to 25 kilograms, were used for the experiments. Following morphine premedication, they were anesthetized with Pentothal sodium and intubated endotracheally. The ventilation during thoracotomy was maintained by a Jefferson respirator. The animals were secured in supine position on a special operating table with a built-in scale. A right anterolateral thoracotomy was performed. The superior vena cava was cannulated through the azygos vein and the inferior cava through the right auricular appendage. Otherwise, the perfusion technique closely resembled that for a human being. Cardiotomy was not performed.

The arterial and central venous pressures, the electrocardiogram, as well as the flow rates, were continuously monitored. By establishing an equilibrium on the table scale before the perfusion began and by following the changes in body weight during extracorporeal circulation, information was gained regarding the intracorporeal blood volume. In selected cases, blood oxygen, carbon dioxide, and arterial pH determinations were performed.

RESULTS AND DISCUSSION

A. *Clinical.*—

The first observations in our perfusions on human beings were made on the behavior of the *arterial pressure.*

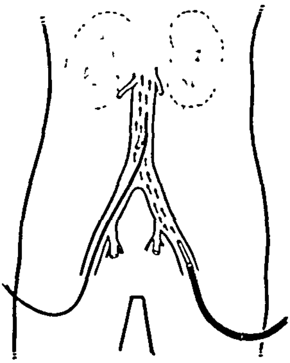


Fig. 1.—The position of the polyethylene pressure monitoring catheter and the arterial perfusion cannula.

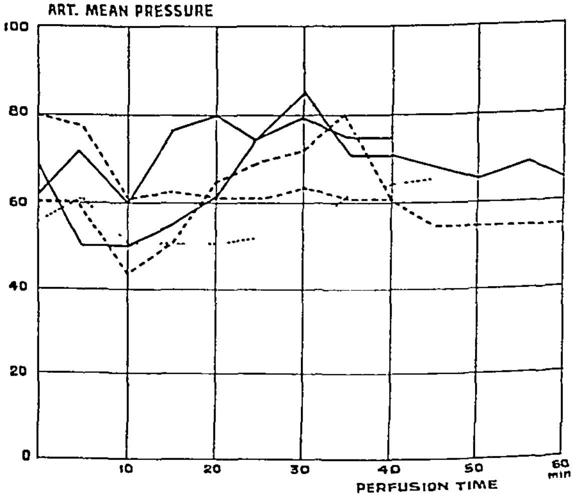


Fig. 2.—The changes in the arterial mean pressure in 5 total body perfusions in human beings (unchanged flow rates).

In a majority of the cases there was no significant drop in the systemic arterial pressure during the surgical procedure preceding extracorporeal circulation. Despite the fact that the perfusions were started with flow rates equal or, in some cases, even exceeding the values of the calculated normal cardiac output, the arterial pressure was below the normal in most of the perfusions and the operations were performed under unwanted hypotension.[13]

In our early cases, by increasing significantly the flow rates, efforts were made to keep the arterial pressure on pre-perfusion levels, but, later, seeing no harmful effects of relatively low arterial pressures (in the presence of normal flow rates), we kept the blood pressure in the femoral artery approximately at a value of 55 mm. Hg.

Abnormally low arterial pressure in the presence of normal blood flow strongly suggests a significant degree of vasodilation immediately at the beginning of the extracorporeal circulation. A dynamic error, however, may also play some part; namely, the opening of polyethylene pressure tap positioned in the direction of the blood stream. Because of the Pitot-effect,[7] there is a possibility that the measured values (P′) were below the level of the actual lateral pressure (P), depending on the velocity (V) of the blood flow

$$P' = P \frac{V^2}{2g} .$$

Calculations and experimental data indicate that this mechanism could be only partially responsible for the measured abnormally low values, and initial

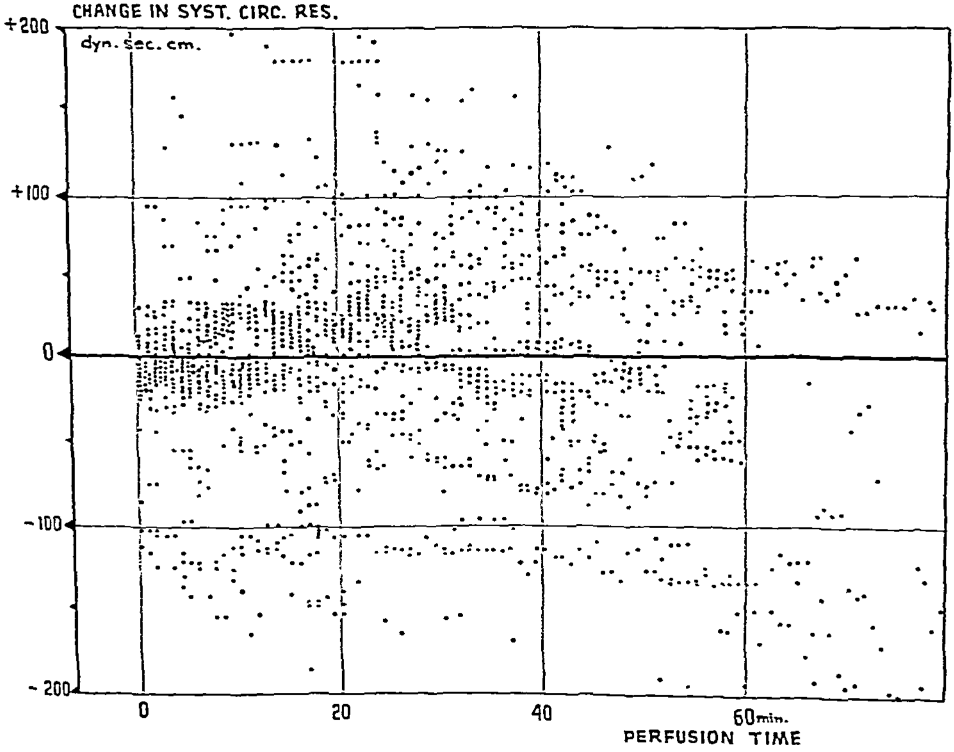


Fig. 3.—The changes in the systemic circulatory resistance in 42 human total body perfusions. The 0 line gives the mean value measured during the first 4 minutes of the cardiopulmonary bypass. Each dot represents a circulatory resistance determination expressed in deviation of this value.

vasodilatation plays a more important role. This is supported by the fact that in animal experiments the decrease of the arterial pressure was accompanied by a simultaneous increase of the intracorporeal blood volume.

Because of the close relationship between flow rate and perfusion pressure, the intra-arterial pressure as isolated data can be evaluated only in the presence of unchanged flow rates.

Fig. 3 shows that changes in the arterial pressure were observed in practically all cases; however, there was a wide individual variation. Usually there was an initial drop in the first few minutes; thereafter, the pressure tended to return to the starting level and, in several cases, exceeded it. In prolonged perfusions, especially in those connected with difficulties in the surgical repair, the pressure tended to decrease again.

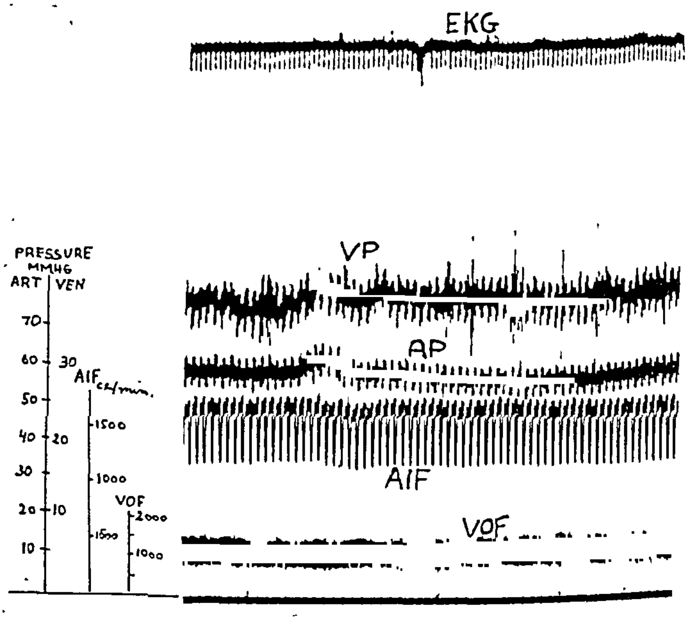


Fig. 4.—A monitoring curve of a patient during cardiopulmonary bypass and open-heart surgery. The improperly selected venous outflow catheters caused an abnormally high venous pressure during the entire perfusion. Note that despite the narrow arteriovenous pressure gradient, the flow rate is satisfactory. *AIF*, arterial inflow; *VOF*, venous outflow.

Naturally extreme changes in the arterial pressure were prevented by re-adjusting the flow rate.

The *venous pressure*, which we regard as the most important guide in the post-perfusion period, remained relatively stabile during perfusion. Until the patient is connected to the extracorporeal circuit, the venous pressure can be determined by two factors, the flow rate and the outflow resistance ($P = R/F$), both of which are regulated mechanically. This means that in the absence of extreme flow rates, the central venous pressure is merely dependent on the venous discharge system (length and diameter of the tubing, size of catheters, siphonage, etc.), rather than the reflection of the dynamic condition of the vascular system.

In all cases in which the perfusion exceeded 5 minutes, the *systemic circulatory resistance* deviated from the starting level. This indicates alterations in the dynamic capacity of the vascular bed, arteriolar dilatation, or opening of the arteriovenous "short-cuts." The change in the systemic resistance varied from moderate to very significant.

The results above show, in the majority of cases, an early vasodilatation, which was replaced by an increase in the resistance (vasoconstriction). In some of the patients this vasoconstrictive phase was followed by a second vasodilatation, usually more significant than the early one.

We had especially interesting experiences in three perfusions. Because of the small size of the venous catheters and inadequate siphonage, the venous pressure remained extremely high during the entire cardiopulmonary bypass. Despite the very narrow arteriovenous pressure gradient, we had no difficulty in perfusing the patients with normal flow rates. This indicates a high degree of vasodilatation and an efficient adaptation of the vascular system to the abnormal situation.

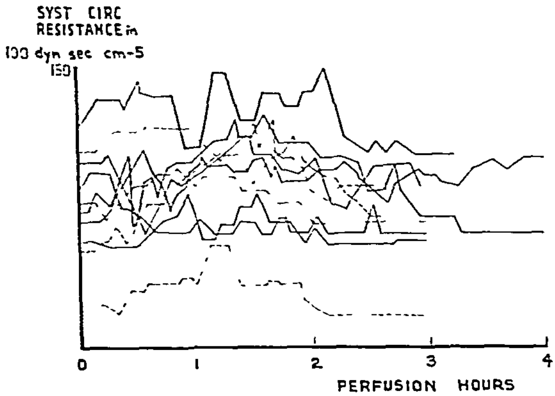


Fig 5.—Changes in the systemic circulatory resistance during prolonged perfusions in dogs.

B. *Experimental.*—

1. *Effects of prolonged perfusions:* The early hemodynamic effects of total cardiopulmonary bypass in dogs were quite similar to those observed in perfusions of human beings. There was an early phase of vasodilation characterized by decrease in the arterial pressure and systemic resistance followed by a vasoconstriction with elevation of the arterial pressure and systemic resistance. The degree of this response varied considerably. In many cases it was intermittent with temporary relapses.

The behavior of the intracorporeal blood volume was peculiar. Because the inflow rate was kept constant during these experiments, the dogs were "free" to take up or give off part of their blood. At the beginning of the perfusion most of the animals took up several hundred cubic centimeters of blood from the extracorporeal system. This was usually followed by repeated shifts in the blood volume from the oxygenator and vice versa.

As time passed, usually more and more blood was retained in the animal. The fact that this happened in part of the experiments without decrease of the systemic resistance or increase of the central venous pressure suggests that the storage of this extra amount of blood was static rather than dynamic, and it was sequestrated in the portal system (Dow) or in other "side-tracks" and did not take an active part in the circulation.

It has been our experience that dogs tolerate prolonged cardiopulmonary bypass poorly, and sooner or later they go into a shock-like condition. Similar observations were made by others who gave different explanations, for example, multiple embolization, bacterial toxemia, absence of the pulsatile flow, anaphylactoid reaction, to name but a few.[5, 6, 10, 21]

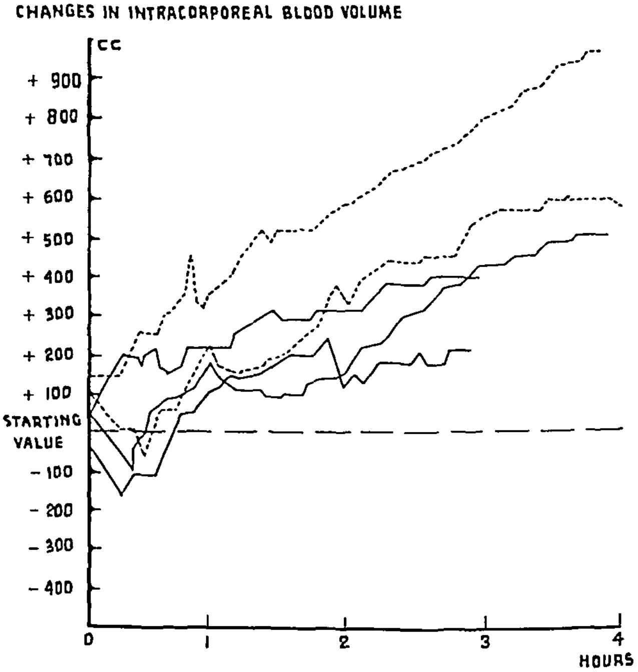


Fig. 6.—Changes in the intracorporeal blood volume during prolonged perfusions in dogs.

Because our study was limited to the simple documentation of the hemodynamic events, rather than to the investigation of their origin, we do not attempt to prove or disprove any of these theories. It is our impression, however, that higher vasomotor centers play an important—primary or interpolated—role in the development of perfusion shock and in the regulation of vascular tonus during perfusion in general.

We came to this conclusion on the basis of the following facts: (a) Significant drop in the arterial pressure and systemic resistance was usually preceded by abnormal changes, in some cases complete flattening of the encephalogram. (b) By closing off the oxygen flow to the oxygenator, hypoxia was induced. The arterial pressure fell simultaneously with the flattening of the electroencephalogram. If the oxygen flow was reopened within 3 to 4 minutes, the electroencephalogram returned to the normal and the arterial pressure

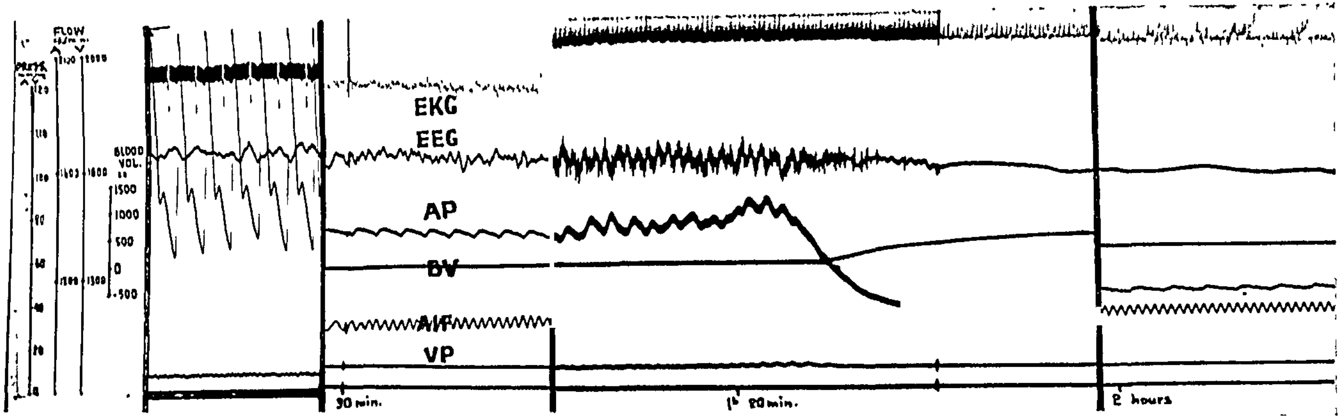


Fig. 7.—Monitoring curve of a total body perfusion in a dog. One hour and 20 minutes after the beginning of the total cardiopulmonary bypass, the EEG became irregular and later completely flat. Simultaneously there was a sudden drop in the arterial pressure. Despite unchanged flow rates and perfect oxygenation, the animal remained in this shock-like condition. *BV*, blood volume; *AIF*, arterial inflow; *AP* and *VP*, arterial and venous pressures, respectively.

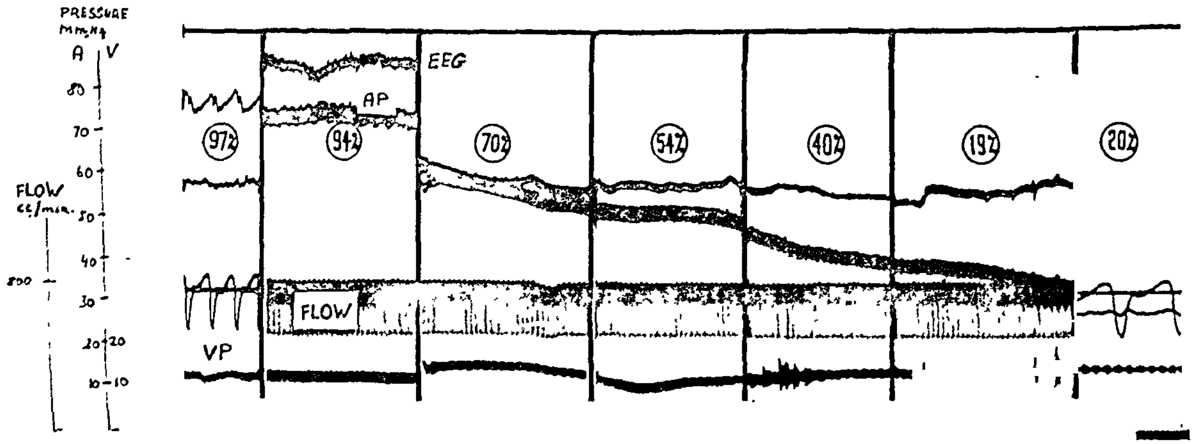


Fig. 8.—Total body perfusion in a dog. Effect of progressive hypoxia. The numbers in circles represent the arterial oxygen saturation. Note the decrease in the intra-arterial pressure (*AP*) and the flattening of the EEG.

rose again. If this hypoxia persisted long enough to cause an irreversible damage of the central nervous system and final cessation of the brain electric activity, the animals went into a permanent shock-like condition characterized

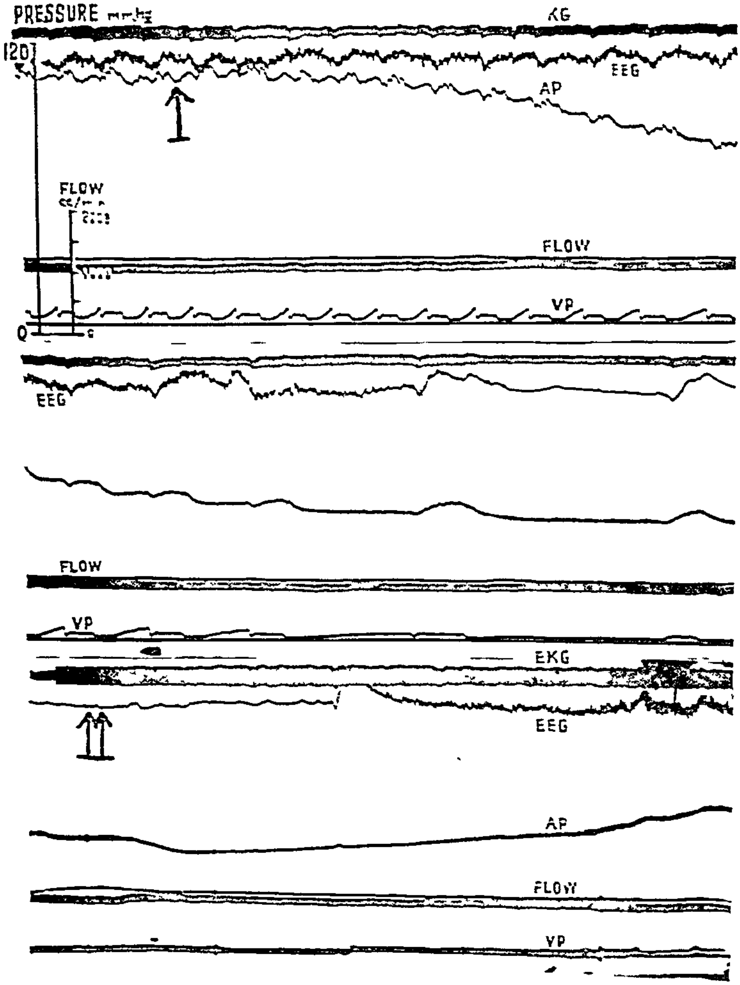
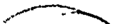


Fig 9—Total body perfusion in a dog Effect of progressive hypoxia and re-oxygenation. The arrow indicates the point where the oxygen flow to the oxygenator was turned off. Note the decrease in the arterial pressure and flattening of the EEG. After the oxygen flow was re-opened (marked by double-arrow) the EEG returned to the normal and the arterial blood pressure rose again

by low arterial pressure, low systemic resistance, and increase of the intracorporeal blood volume.

2. *Certain pharmacologic effects:* The administration of vasoactive agents during extracorporeal circulation induced an immediate and vigorous hemodynamic response.

Adrenaline, 0.01 mg. per kilogram, injected into the arterial line of the circuit caused a marked increase in the systemic resistance and a high degree of arterial hypertension.



Other hemodynamic effects of the administration of Adrenaline were: increase of the venous outflow from the animal, temporary increase and then decrease of the venous pressure, and decrease of the intracorporeal blood volume. We suppose that in the production of these effects the emptying of the static blood reservoirs of the body (spleen, etc.) may also play some role.

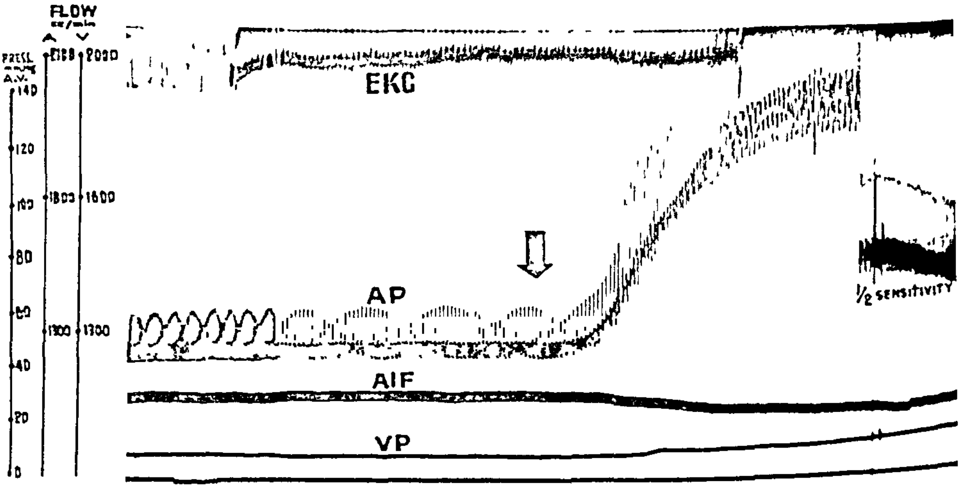


Fig. 10.—Total body perfusion in a dog. Effect of intra-arterial injection of Adrenaline. Note the extreme increase in the arterial pressure *(AP)*, increase in the venous pressure *(VP)*, and moderate decrease in the arterial inflow *(AIF)*.

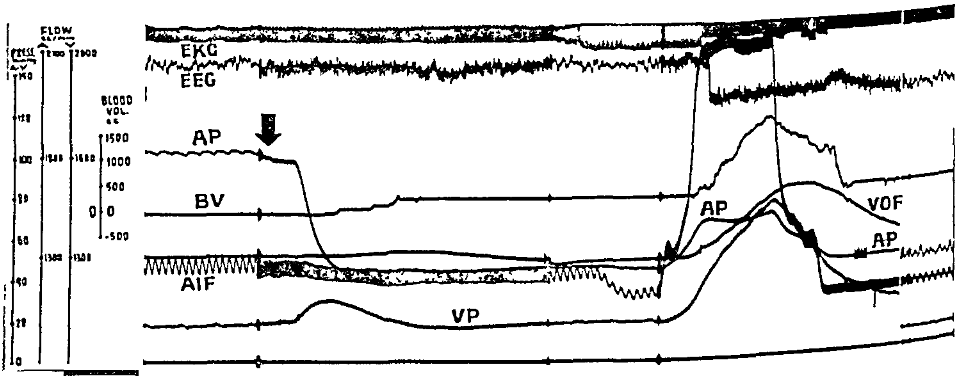


Fig 11.—Total body perfusion in a dog. Effect of intra-arterial injection of Thorazine. Note the drop in the arterial pressure *(AP)*. The original level of the arterial pressure could not be restored even by increasing the arterial inflow *(AIF)* threefold. *VOF*, venous outflow; *BV* blood volume, *VP* venous pressure.

Chlorpromazine (Thorazine), 1 mg. per kilogram, injected into the return line caused a marked fall in the sytemic resistance and arterial pressure and a moderate increase in the venous pressure and intracorporeal blood volume. These effects were of long duration and the arterial pressure did not return to the initial level even by increasing the flow rate threefold. The arterial pressure, however, did not fall below 50 mm. Hg and the arterial oxygen saturation remained unchanged.

Clinically, it might be important to note that the animals given Thorazine did not show any further significant fluctuation in arterial pressure and systemic resistance; however, their intracorporeal blood volume still increased during prolonged perfusion.

3. *Hemodynamic effects of excessive flow rates:* Using progressively increasing flow rates we found the vascular system of the dog highly adaptable. The common denominator of this reaction was vasodilatation to the increase and vasoconstriction to the decrease of blood flow. This response, however, had its "lower" and "upper limits." For simplification we accepted a flow rate with a value of 80 c.c. per minute per kilogram of weight as an arbitrary normal. With perfusion of the dogs with this rate, as mentioned previously, the blood pressure remained on a somewhat normal level.

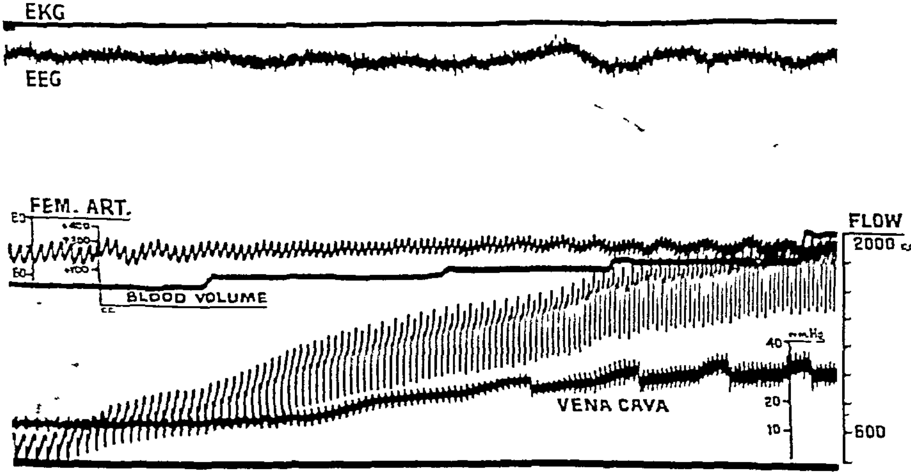


Fig. 12.—Total body perfusion in a dog. Effect of progressively increasing flow rates. Note that despite the significant increase in flow (pulsating curve), the pressure in the femoral artery remains practically the same.

The diminution of the flow rate below this value caused only a moderate or no decrease in the arterial pressure but a marked increase in the systemic resistance. The further diminution of the flow rate caused a collapse of this adaptation with marked pressure drop and no increase in the resistance.

The fact that Adrenaline caused elevation of the blood pressure, even in this situation, indicates that vasoconstriction at low flow rates is not maximal.

Flow rates moderately higher than normal did not raise the arterial pressure. In some experiments the flow rate was increased twofold without causing a significant pressure elevation. This could be explained only by an immediate diminution of the systemic resistance. Further elevation of flow rate caused increase in the arterial and venous pressures, additional decrease of the systemic resistance, and increase of the intracorporeal blood volume.

Finally, at extreme flow rates, a significant outflow deficit developed with arterial and phlebohypertension and fixed systemic resistance. This could be attributed to the possibilty that the dilatation (distention?) of the vascular tree reached its maximum and at these flow rates it behaved as a rigid system.

4. *Effects of constriction of the venous outflow:* To study the time element in the vasomotor response, experiments were performed in which the venous outflow from the animals was suddenly constricted. This caused a progressive and rapid increase of the venous pressure and intracorporeal blood volume, moderate increase in the arterial pressure, and an immediate drop in the systemic resistance.

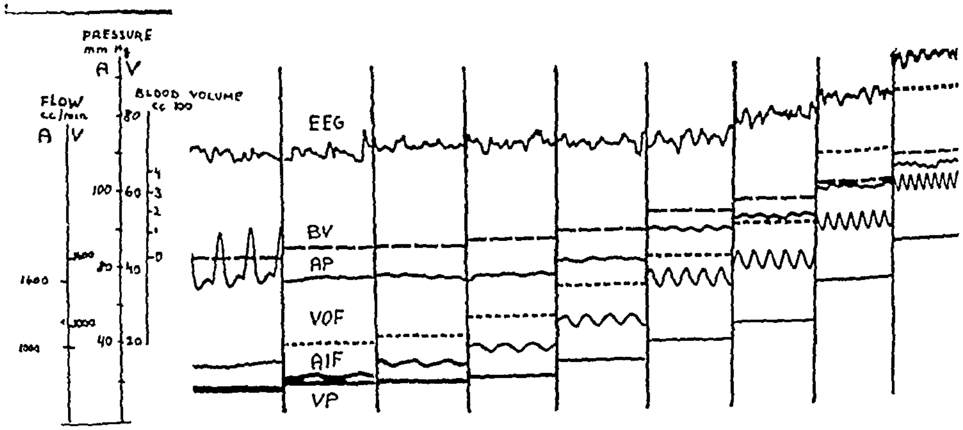


Fig 13.—Total body perfusion in a dog Effect of progressively increasing flow rates The increase in the arterial inflow (*AIF*) causes progressive increase in the venous outflow (*VOF*), blood volume (*BV*), venous pressure (*VP*) Note that the arterial pressure increases only at extreme flow rates, and the arteriovenous pressure difference decreases proportionally to the increase in the arterial inflow

Within a short time, the venous pressure reached extremely high levels If at this time the constriction was suddenly released, the reverse of the previous chain of events occurred with high venous outflow rates and progressive return of the venous pressure and blood volume to the pre-occlusion levels.

The arterial pressure behaved in a peculiar manner. Immediately after the release of the occlusion, the pressure dropped *below* the pre-occlusion level, and then returned to this value. The possible explanation for this phenomenon follows.

The occlusion of the outflow caused a circulatory overload and an immediate vasodilatation (distention?) of a high degree. After the constriction was released and the overloaded vascular system drained, a sudden discrepancy developed between the unchanged flow rate and the maximally dilated vascular system. The return of the arterial pressure to the pre-occlusion level indicated the re-establishment of the vascular tone and pressure flow-resistance equilibrium.

SUMMARY

Observations made during open-heart operations indicate that there are changes of unknown origin in circulatory dynamics during total body perfusion.

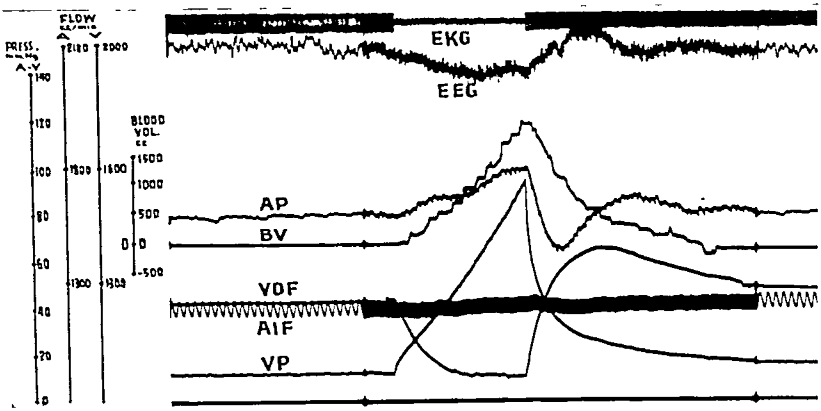


Fig. 14.—Total body perfusion in a dog. Effect of the constriction of the venous outflow line. The constriction is followed by a decrease in the venous outflow *(VOF)*, increase in the venous pressure *(VP)*, increase in the intracorporeal blood volume *(BV)*, and increase in the arterial pressure *(AP)*. The release of the constriction causes a temporary drop in the arterial blood pressure *below* the starting level. Arterial inflow *(AIF)* unchanged.

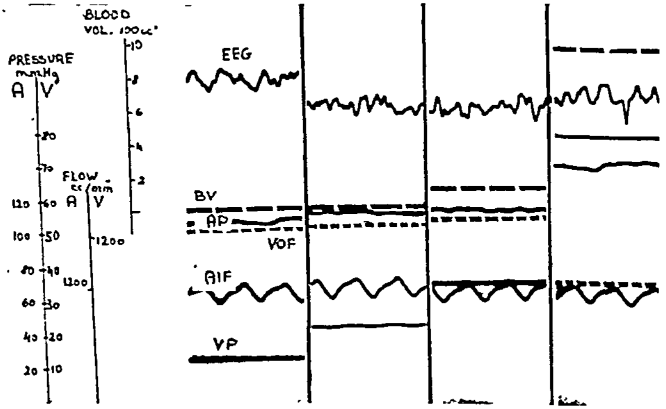


Fig. 15.—Total body perfusion in a dog. Effect of the increase in the venous outflow resistance (progressive elevation of the venous outflow reservoir). The arterial pressure *(AP)* increases only after the decrease of the venous outflow *(VOF)*. *VP*, venous pressure; *BV* blood volume; *AIF* arterial inflow.

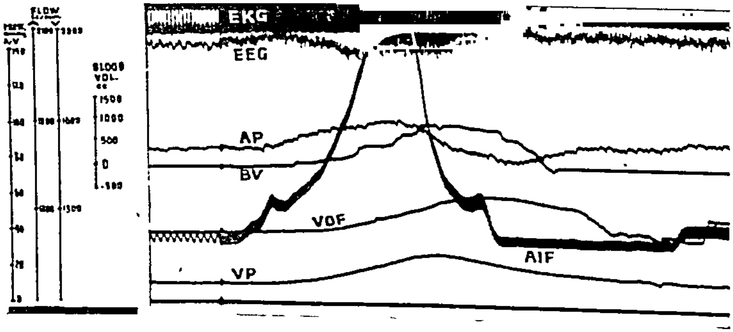


Fig. 16.—Total body perfusion in a dog. Effect of the acute overperfusion. *AIF*, arterial inflow; *VOF*, venous outflow; *VP*, venous pressure. Note that the arterial pressure *(AP)* increases only moderately, and there is no change in the arteriovenous pressure difference. Note also the temporary drop in the arterial pressure after the flow rate was returned to the starting level.

The perfusion pressure fluctuates despite unchanged flow rate; on the other hand, if efforts are made to keep this pressure constant, the flow rate has to be readjusted repeatedly. There are also unexplained shifts in the blood volume from the patient to the extracorporeal circuit and vice versa

To investigate these phenomena the authors studied the hemodynamics during complete cardiopulmonary bypass in 42 perfusions of human beings and in a series of animal experiments.

Despite calculated "normal" perfusion rates, the arterial pressure stayed at subnormal levels and varied considerably in most of the human perfusions Usually there was an indication of an early vasodilatation followed by a vasoconstrictive phase. If the cardiopulmonary bypass was prolonged, these phases were followed by a second–more pronounced–vasodilatation.

Animal experiments showed that the circulatory system of the dog reacted strongly to pharmacologic agents and to anoxia during total body perfusion. Low flow rates caused vasoconstriction with overload of the circulatory system by abnormally high flow rates, or, by outflow constriction, they led to marked vasodilatation.

REFERENCES

1. Andersen, M. N., and Senning, A.: Studies in Oxygen Consumption During Extracorporeal Circulation With a Pump-Oxygenator, Ann. Surg. 148: 59, 1958.
2. Blair, E., Zimmer, R., and Martin, L.: Hemodynamic Effects of Total Circulatory Occlusion During Hypothermia, Surg. Gynec. & Obst. 108: 13, 1959.
3. Boyd, A. D., Tremblay, R. E., Spencer, F. C., and Bahnson, H. T.: Estimation of Cardiac Output Soon After Intracardiac Surgery With Cardiopulmonary Bypass, Ann. Surg 150: 613, 1959.
4. Dodrill, F. D., Marshall, N., Nyboer, J., Hughes, C. H., Derbyshire, A. J., and Stearns, A. B.: The Use of the Heart-Lung Apparatus in Human Cardiac Surgery, J. Thoracic Surg. 33: 60, 1957.
5. Dow, J. W., Dickson, J. F., III., Hamer, N. A. J., and Gadboys, H. L: The Effects of Anaphylactoid Shock From Blood Exchange on Cardiopulmonary Bypass in the Dog, J. Thoracic Surg. 39: 457, 1960.
6. Dow, J. W., Dickson, J. F., III., Hamer, N. A. J., and Gadboys, H. L.: Anaphylactoid Shock Due to Homologous Blood Exchange in the Dog, J. Thoracic Surg. 39: 449, 1960.
7. Fry, D. L.: Certain Aspects of Hydrodynamics as Applied to the Living Cardiovascular System, IRE Tr. Medical Electronics 4: 252, 1959.
8. Galetti, P. M., Nickerson, W. L., and Brecher, G. A.: Cardiovascular Adaptation to Partial Extracorporeal Circulation, Tr. Am. Soc. Artificial Int. Organs 5: 191, 1959
9. Gross, R. E., Sauvage, L. R., Pontius, R. G., and Watkins, E., Jr.: Experimental and Clinical Studies of a Siphon-filling Disc Oxygenator System for Complete Cardiopulmonary Bypass, Ann. Surg. 151: 285, 1960.
10. Hardaway, R. M., and McKay, D. G.: Intravascular Thrombi and the Intestinal Factor of Irreversible Shock, Ann. Surg. 150: 261, 1959.
11. Head, L. R., Coenen, J. P., Angola, E., Noguiera, C, Mendelsohn, D., and Kay, E B.: Operation of the Roller Pump for Extracorporeal Circulation, J. Thoracic Surg 39: 210, 1960.
12. Kay, E. B., Galajda, J. E., Lux, A., and Cross, F. S.: The Use of Convoluted Discs in the Rotating Disc Oxygenator, J. Thoracic Surg. 36: 268, 1958.
13. McGoon, D. C., Moffitt, E. A., Theye, R. A., and Kirklin, J. W.: Physiologic Studies During High Flow, Normothermic, Whole Body Perfusion, J. Thoracic Surg 39: 275, 1960.
14. Mendelsohn, D., Jr., MacKrell, T. N., MacLachlan, M. A., Cross, F. S., and Kay, E. B.: Experiences Using the Pump Oxygenator for Open Cardiac Surgery in Man, Anesthesiology 18: 223, 1957.
15. Merendino, K. A., Thomas, G. I., Jesseph, J. E, Herron, P. W., Winterscheid, L C, and Vetto, R. R.: The Open Correction of Rheumatic Mitral Regurgitation and/or Stenosis, Ann. Surg. 150: 5, 1959.

16. Moffitt, E. A., Patrick, R. T., Swan, H. J. C., and Donald, D. E.: A Study of Blood Flow, Venous Blood Oxygen Saturation, Blood Pressure and Peripheral Resistance During Total Body Perfusion, Anesthesiology 20: 18, 1958.
17. Kuhn, L. A., Gruber, F. L., Frankel, A., and Kupfer, S.: Hemodynamic Effects of Extracorporeal Circulation in Closed Chest Animals and in Those With Myocardial Infarction With Shock, Circulation Res. 8: 199, 1960.
18. Robicsek, F., Sanger, P. W., and Taylor, F. T.: A Blood Flowmeter for Extracorporeal Surgery, Surgery 46: 396, 1959.
19. Robicsek, F.: Orifice-Plate Flowmeter for Extracorporeal Circuit, IRE Tr. Medical Electronics 4: 249, 1959.
20. Sanger, P. W., Taylor, F. H., Robicsek, F., Dvorak, J. J., and Stam, R. E.: Experiences With Direct-Vision Repair of Congenital Cardiovascular Disorders Using the Rotating Disc Oxygenator, North Carolina M. J. 20: 89, 1959.
21. Sanger, P. W., Taylor, F. T., Robicsek, F., Stam, R. E., and Dvorak, H. J.: Some Problems in Open Heart Surgery, Am. Surgeon 25: 578, 1959.
22. Takaro, T.: Personal communication.
23. Waldhausen, J. A., Ross, J. J., Jr., Lombardo, C. R., Cooper, T., Gilbert, J. W., and Morrow, A. G.: Flow and Volume Regulation During Cardio-Pulmonary By-Pass; The Use of an Electromagnetic Flowmeter and a Device for Automatic Control of Oxygenator Volume, Tr. Am. Soc. Artificial Int. Organs 5: 172, 1959.
24. Wesolowski, S. A., Sauvage, L. R., and Pinc, R. D.: Extracorporeal Circulation: The Role of the Pulse in the Maintenance of the Systemic Circulation During Heart-Lung By-Pass, Surgery 37: 663, 1956.

DISCUSSION

DR. LEWIS H. BOSHER, Richmond, Va.—We have been concerned with some of the problems presented in Dr. Sanger's interesting paper in our efforts to maintain a more physiologic perfusion.

We have recently employed an apparatus constructed by Mr. Jack Edwards which automatically adjusts flow rates to the varying requirements occurring during open-heart surgery. It is commonly advocated that the clinical perfusion be conducted on a basis of a constant arterial flow rate. Under our present method, employing a closed loop servomotor system, a selected arterial pressure is set on the control panel. Any deviation from this pressure causes an error signal to be applied to a sensitive amplifying system driving a reversible pump, which operates between a transfusion reservoir and a "T" fitting in the venous line.

(Slide) We have a gauge connected into the patient's arterial system which will then be matched against a pressure set on the control panel, so that an error detection is supplied to the servomotor system. This energizes the system in such a way that through a sensitive amplifying system a signal is delivered to the motor controlling a transfusion pump, which is reversible and can supply blood as well as take it away from the system. If the pressure drops below the present level, blood is delivered to the system which restores the pressure to that selected by the pump operator.

The adjustments are rather rapid and accurately made. It is believed that the superior performance of this apparatus may be particularly realized in certain difficult perfusions, such as those on tiny infants and those in which large blood losses occur from the vascular bed of the patient.

DR. GEORGE H. A. CLOWES, JR., Cleveland, Ohio.—In many respects the data which Dr. Sanger's paper contained provide amplification and confirmation of work which has gone before.

Having recently completed a review on the artificial maintenance of circulation—rather an extensive one—for *Physiological Reviews,* I should like to pass on to you certain of the hemodynamic concepts in relation to perfusion of the entire body which became increasingly clear to me while doing this. It is necessary to consider this in two parts: partial perfusion and, in contrast, total perfusion. During the former, the normal cardiovascular regulatory mechanisms are at work as shown clearly by Galetti and Brecher. When all the blood returning to the right heart is diverted into the extracorporeal system to be pumped back into the arterial system, an entirely different set of circumstances exists, as indicated by the early work of Herron, Jesseph, and Merindino and that of Donald and Moffitt. The normal regulatory reflexes initiated within the heart and vessels of the lesser circulation are eliminated

Because of the limitations of cannulation, blood flows during total perfusion of the whole body which are greater than resting basal values are seldom attained. Within the range generally used in this work, the arterial pressure is nearly linear in its relation to the perfusion rate. At very high rates, when the aortic and carotid depressor nerves become activated, the resistance decreases. At very low flow rates, when hypoxia occurs and catecholamines are secreted into the blood, the resistance increases somewhat. By the injection of ganglionic blocking agents and Arfonad in the course of perfusions, Read was able to show that vasomotor activity, both intrinsic and neurogenic, plays a part in the maintenance of this vascular resistance. This is further influenced by the presence of acidosis and hypoxia as well as by damage to blood elements.

Further, the venous return, which is in great measure responsible for the regulation of cardiac output under normal circumstances by alteration of venous tone and shifts of blood from storage areas, is also directly related to the rate at which an artificial perfusion can be maintained. Even though the pressure in the venea cavae be kept constatnt, a reduction of 10 per cent in blood volume causes a 50 per cent fall of venous return and pump output This can be altered temporarily by the injection of norepinephrine which constricts the venous system and increases the pressure and rate of return. The intracorporeal blood volume is further augmented by hypothermia Thus, it appears that, although the arterial system behaves in a manner resembling the normal during perfusion, the control of the venous side is upset by the absence of the normal reflexes initiated by the baroreceptors in the atria, ventricles, and pulmonary vessels Thus, it has been stated that during total perfusion the vessels behave like a set of distensible rubber tubes.

Dr. Sanger has presented most interesting data showing the type of changes in hemodynamics which take place over a prolonged period of time during perfusions at a medium rate. Daly, in England, has drawn attention to the increase of resistance which he has shown This, Daly believes, is related to the release of "vasotonins" which comes from damaged blood elements Only late in the course of a prolonged perfusion is this trend reversed, as damage to small vessels and organs takes place The work of Dr Sanger and his associates, in my opinion, is of great value for its care in documenting this phenomenon as well as the useful instrumentation employed.

DR ELTON WATKINS, JR., Boston, Mass—We all have observed changes of a type similar to Dr Sanger's in human perfusion and have found that, in order to maintain what we regarded as adequate pressures, occasionally we have to increase flow two or three times greater than we expected. For this reason, because of the transitory changes in the vasomotor activity, or whatever causes these flow pressure ratio alterations, we have utilized two precautions in our perfusions.

First, we like to have a large volume of priming blood in our machine to give us a little leeway in pump operation when these changes occur.

Second, we spend a great deal of time on partial bypass before going on total bypass, even when things appear to be going well. We may spend 15 minutes doing partial perfusion We find that these changes occur less strikingly after a lengthy period of partial bypass

I'm wondering if we can conclude from Dr Sanger's data what the mechanism of these real changes are. I'm not exactly clear as to the reason why Dr. Sanger—and I hope that he will elaborate on it for me—why he believes that these vasomotor changes may be central in origin. The electroencephalographic tracings in the slides show changes that are starting several seconds after the initial change in the blood pressure tracings, and I am wondering which is cause and which is effect in these tracings

DR. DAVID LONG, Minneapolis, Minn.—We have also been interested in the changes that have been described by Dr. Sanger and others during extracorporeal circulation. In addition, we have attempted to add more to this study by making some observations of the microcirculation, or the circulation in the precapillary arterioles, the capillaries, and the postcapillary venules.

We have found that this is probably a very valuable approach to the problem, since, actually, the microcirculation is the best reflection of tissue perfusion or cellular perfusion that we can assess. Changes that occur in the pressure and peripheral resistance in the large vessels are not necessarily reflective of changes that occur in the smaller vessels and in the capillaries.

The observations that we have documented with this type of study have been correlated with the changes in peripheral resistance: namely, we have found in the perfusion—and particularly during prolonged perfusion—that there is a marked vasoconstriction of the small arterioles, a closing off of large segments of the capillary bed, and the appearance of microscopic arteriovenous shunts.

In addition, another interesting observation is that, if the perfusions have been prolonged in animals and in patients, there is clumping of red blood cells or intravascular aggregation which results in the obstruction of flow in the capillaries and the postcapillary venules. We have found that some of these changes are preventable by administration of low molecular weight dextran or dextran of an average molecular weight of about 41,000. The corresponding microscopic changes of ischemia in vital organs, such as the kidney, liver, and heart, have been partially or totally prevented.

DR. GEORGE MAGOVERN, Pittsburgh, Pa.—We, too, have observed changes in blood pressure during extracorporeal circulation. However, it has been our experience that if we maintain a normal venous pressure during the perfusion, arterial pressure will not be as variable.

We have noted on occasion, when maintaining a venous pressure of 7 or 8 mm. Hg, that lowering the venous pressure without changing the flow rate or possibly increasing it a little, one can observe a fall in the blood pressure of 10 or 15 points. We believe that by maintaining a normal venous pressure, we increase the stability of the whole vasomotor system, avoiding the fluctuations which were observed by Dr. Sanger.

DR. ARTHUR M. VINEBERG, Montreal, Quebec.—During the past 2 years we have been studying blood volume changes and other hematologic changes both in the animal and in man. Part of our interest has been stimulated by the question of long perfusion, particularly with the aim in mind of supporting circulation in coronary shock. In our experimental work we have found evidence of vasoconstriction during perfusion. For example, it has been observed that there is no urinary output 45 minutes to 1 hour after a partial perfusion, which consists of withdrawing blood from the femoral vein and returning it to the femoral artery, after it has been passed through an oxygenator. In this type of perfusion with the chest closed, we find that the animals do not do well when more than 20 to 25 per cent of the total blood volume is circulated through the extracorporeal unit. We have had only 2 animals survive a 6-hour partial perfusion, using 25 per cent of their total circulating blood volume. Most animals recover consciousness but manifest extreme weakness and die during the night. We think that the same vasoconstrictor mechanism which prohibits urinary secretion may cause ischemia of the adrenal gland. There is a possibility that ischemia of the adrenal glands may be responsible for the marked prostration which occurs in the animals after prolonged partial perfusion. This aspect of the problem is now being studied.

DR. ROBICSEK (Closing).—First, I would like to answer Dr. Bosher's remarks. We certainly want to congratulate him for this ingenious device. It is our opinion that it is not too good to overautomize, and I think we will agree that it is the best to leave the final word to the person who monitors the pump.

In answer to Dr. Clowes, I am very thankful for these remarks. We knew most of these data from the literature, reported by Daly, Luolany, and Petrovskaia, and it was described before Daly by Starling. Most of these are well known physiologic facts.

We did not try to rediscover these observations, what we tried to say is only that vaso motor activity is going on during perfusions. We didn't do extensive research as to why and what triggers this mechanism, but it is interesting that if we set a constant flow rate for a patient, there are significant changes in blood pressure, which vary from 5 mm. Hg to 25 or 30 mm. Hg. If this is done in dog experiments, inevitably the dogs go into shock after 4 or 5 hours of pumping—probably because of hematologic changes, but there are probably a lot of other factors as well. We did not investigate these factors. We just tried to describe the changes.

Also, if you put a patient on the pump oxygenator, the blood pressure level rises and decreases and rises again, and finally decreases again. So everything indicates that the body is doing something. We don't know exactly what it is, but we think and we hope that it knows what it is doing.

Now, regarding the proportions of the flow, it is natural that the arterial pressure finally rises if the flow is raised above the limits, but there is not a direct relationship. One can raise the flow in some cases by 50 per cent without having any effect on the arterial pressure.

I think the venous pressure itself expresses the flow more clearly, because primarily the pressure is related to the flow and the resistance. The arterial resistance is changeable—elastic—and has many biologic elements, catecholamines and other things; but the venous pressure is related to the flow and to the mechanical outflow resistance alone.

Regarding Dr. Watkins' remarks, we too are fearful people and we have a lot of blood in reserve, close to the heart-lung machine, when we start to operate, and we fully agree with his advice of putting a patient in a partial bypass before starting the full bypass. Very often we get into some kind of trouble. If it is not perfectly clear when the patient is overperfused or underperfused, if we leave the pump running in partial bypass, the patient himself usually compensates for the changes in blood volume.

AN EXPERIMENTAL EVALUATION OF OPERATIONS FOR REVASCULARIZATION OF THE HEART

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For the past 3 years, our group has conducted an experimental evaluation of procedures presently in clinical use for the revascularization of the heart.[1-5] We have performed seven different types of operations on dogs. These operations were the ligation of the internal mammary arteries, the phenol-talc-lingula procedure and its individual components, a phenol procedure, a talc procedure, and a lingula procedure, and subclavian and carotid arterial implantations. After the initial revascularization operation, a minimum period of 3 months elapsed prior to reoperation and measurement of the coronary flow.

METHODS

As controls, 8 dogs have been subjected to a left thoracotomy, opening of the pericardium for 1 minute, and then closing it loosely. The chest was then closed in routine fashion.

Ligation of the internal mammary artery was accomplished by two cutdowns just lateral to the sternum in the third intercostal space and ligation of the arteries distal to the pericardiophrenic branch. The cutdowns were then closed.

The phenol-talc-lingula procedure required a left thoracotomy in the fifth intercostal space and opening of the pericardium. The epicardium was abraded with 90 per cent phenol, as was the inner side of the pericardium. One and a half grams of talc was then applied to the abraded epicardium. The lingula was tacked over the abraded epicardium and the pericardium was loosely closed over it. The chest was closed in routine fashion.

Each of the phenol, the talc, and the lingula operations was performed in the same manner as the phenol-talc-lingula procedure but with only the single component carried out.

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The subclavian arterial implants were performed through a left thoracotomy in the fourth intercostal space, and the left subclavian artery was dissected free for several centimeters and tied. The proximal stump of several centimeters in continuity with the aorta had multiple perforations put in its distal segment. It was then pulled through a myocardial tunnel fashioned after the method of Vineberg.[1]

The carotid implants were performed with the same method as the subclavian implants except that the carotid artery was dissected out in the neck for several centimeters and was then brought through a small hole in the apex of the left pleural cavity and placed in a myocardial tunnel. The carotid transplant was performed by dissecting the artery free for several centimeters and removing it entirely from the neck. It was transplanted in the thorax by anastomosing it end-to-side to the thoracic aorta and bringing its free segment through the myocardial tunnel. Sterile technique was used in all cases.

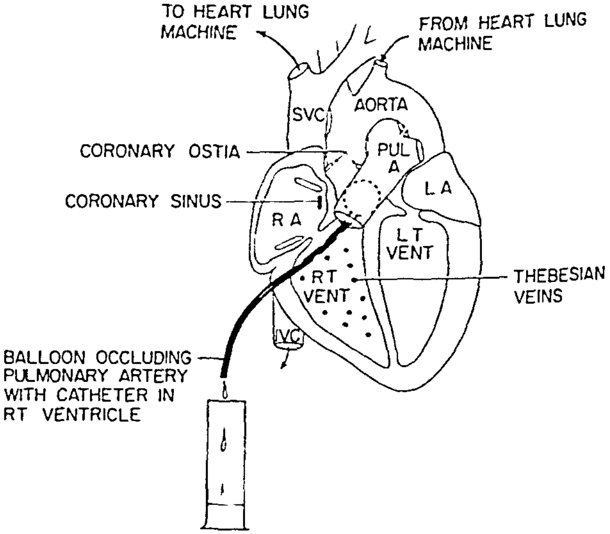

Fig 1 —Technique for measuring the coronary flow with modified Foley catheter.

After a minimal period of 3 months, the animals underwent open-heart surgery in order to measure coronary flow by a method previously described by our group.[6] Two Sigmamotor pumps and a simple bubble oxygenator were used.[7] The animals were placed on total extracorporeal bypass. Both pulmonary hila were clamped to prevent bronchial flow from entering the left heart and subsequently the coronary ostia. A modified Foley catheter was inserted through a small right ventriculotomy into the pulmonary artery and the balloon was inflated occluding the artery. The Foley catheter was modified by ligating the tip of the catheter distal to the balloon and by cutting three holes proximal to it. The catheter then provided drainage for all the coronary return from the coronary sinus and Thebesian veins entering the right ventricle (Fig. 1).

The coronary venous return was collected in a graduate and several 1-minute samples were measured. The aorta was then cross-clamped 3 cm. beyond the aortic valve so that arterial blood from the extracorporeal unit could not reach the coronary ostia. It was then presumed that all blood recovered from the right side of the heart had arrived through collateral channels provided in the revascularization procedure. To substantiate this assumption, the channels provided in the revascularization procedure were destroyed by stripping adhesions or clamping an implant. If flow promptly dropped to control levels that have been determined in control animals, the revascularization operation was believed responsible for the additional flow.

RESULTS

Fifty-six animals underwent both the revascularization procedure and the evaluation operation. Eight of these animals with control operations gave us our baseline data. At the time of reoperation on these 8 animals, the following data were compiled (Table I).

TABLE I. CORONARY FLOW

DOG NUMBER	AORTA OPEN (C.C./MIN.)	AORTA CLOSED (C.C./MIN.)	PER CENT FLOW
927	65	1.0	1.5
818	91	0.5	0.5
933	92	0.4	0.5
898	42	0.6	1.4
1061	130	0.7	0.8
1205	77	0.3	0.4
1135	186	0.0	0.0
1424	51	1.0	2.0
Averages	92	0.6	0.6

There were 8 animals with internal mammary artery ligations. Of these 8 animals, 2 showed a flow slightly in excess of the control animals (Table II).

TABLE II. CORONARY FLOW

DOG NUMBER	AORTA OPEN (C.C./MIN.)	AORTA CLOSED (C.C./MIN.)	PER CENT FLOW
926	130	0.85	0.6
925	54	1.4	2.5
903	80	2.4	3.0
930	78	0.8	1.0
931	77	1.4	1.8
932	55	0.0	0.0
852	115	0.25	0.2
855	115	0.5	0.48
Averages	88	0.94	1.2

The phenol-talc-lingula procedure was performed on 7 animals, 4 of which had a flow in excess of control levels (Table III).

There were six lingula operations. In 2 of these animals, there was a sizable flow after clamping the aorta. We believe this flow was bronchial in nature because the left hilum could not be clamped in this category. In both of these cases there was little change in flow after stripping the lingula from

TABLE III. CORONARY FLOW

DOG NUMBER	AORTA OPEN (C.C./MIN.)	AORTA CLOSED (C.C./MIN.)	ADHESIONS STRIPPED	DIFFERENCE (C.C./MIN.)	PER CENT FLOW
897	75	3.1	0.5	2.6	3.5
902	118	2.8	0.3	2.5	2.1
906	66	0.0	0.0	0.0	0.0
862	112	0.2	0.2	0.0	0.0
893	115	4.8	0.3	4.5	3.8
1008	91	0.0	0.0	0.0	0.0
1019	84	7.4	1.9	5.5	6.5
Averages	94	2.6	0.5	2.2	2.3

the surface of the heart, indicating that the flow was not coming through the adherent lingual. Dog No. 1167 presented puzzling data in that the coronary flow increased after stripping the lingula from the surface of the heart (Table IV).

TABLE IV. CORONARY FLOW

DOG NUMBER	AORTA OPEN (C.C./MIN.)	AORTA CLOSED (C.C./MIN.)	LINGULA STRIPPED	DIFFERENCE (C.C./MIN.)	PER CENT FLOW
1136	66	8.0	8.0	0.0	0.0
1149	75	0.8	0.8	0.0	0.0
1154	92	0.4	0.2	0.2	0.3
1167	78	1.6	4.3	-2.7	0.0
1168	70	14.8	13.7	1.1	1.7
1189	120	0.3	0.0	0.3	0.2
Averages	83.5	4.3	4.5	0.3	0.4

Seven animals underwent a talc poudrage. Only 2 animals in this category demonstrated a flow in excess of control values (Table V).

TABLE V. CORONARY FLOW

DOG NUMBER	AORTA OPEN (C.C./MIN.)	AORTA CLOSED (C.C./MIN.)	ADHESIONS STRIPPED	DIFFERENCE (C.C./MIN.)	PER CENT FLOW
1103	63	0.8	0.8	0.0	0.0
1117	134	0.3	1.0	-0.7	0.0
1157	57	0.5	0.5	0.0	0.0
1159	100	5.9	2.0	3.9	3.9
1161	62	0.8	0.8	0.0	0.0
1181	49	1.0	0.0	1.0	2.0
1182	71	1.0	0.8	0.2	0.4
Averages	77	1.5	0.8	0.7	0.9

Eight animals had a phenol procedure performed. Three of these animals showed flow in excess of the control levels (Table VI).

TABLE VI. CORONARY FLOW

DOG NUMBER	AORTA OPEN (C.C./MIN.)	AORTA CLOSED (C.C./MIN.)	ADHESIONS STRIPPED	DIFFERENCE (C.C./MIN.)	PER CENT FLOW
1132	63	1.5	0.0	1.5	2.3
1129	162	4.4	0.0	4.4	2.7
1146	76	0.8	0.2	0.6	0.8
1163	39	0.3	0.0	0.3	0.8
1165	97	0.8	0.8	0.0	0.0
1095	62	0.7	0.2	0.5	0.8
1097	112	0.8	0.3	0.5	0.4
1092	48	4.1	0.7	3.4	7.0
Averages	82	1.7	0.3	1.4	1.85

A total of 13 arterial implants were performed. Four of these were subclavian implantations. Seven were carotid implants, and, in 2 animals, the carotid artery was used as an autograft from the descending thoracic aorta into the left ventricular wall.

None of the subclavian implants significantly contributed to the coronary flow. Only two of these implants were found patent at autopsy. Two of the carotid implants provided increased coronary flow and one of the carotid transplants showed an increased coronary flow. Three of the carotid implants which did not provide an increase in flow were found at autopsy to have undergone thrombosis. The pulmonary hila were not clamped in the first 8 animals listed in Table VII.

TABLE VII. CORONARY FLOW

DOG NUMBER	AORTA OPEN (C.C./MIN.)	AORTA CLOSED (C.C./MIN.)	IMPLANT CLAMPED	DIFFERENCE (C.C./MIN.)	PER CENT FLOW	PATENT IMPLANT
s.* 799-02	76	0.8	0.8	0.0	0.0	yes
s. 839	80	1.1	1.1	0.0	0.0	no
s. 849	162	0.4	0.4	0.0	0.0	no
s. 870	66	0.18	0.0	0.18	0.2	yes
c. 939	134	7.4	7.4	0.0	0.0	yes
c. 889	109	6.6	6.6	0.0	0.0	yes
c. 985	79	2.7	4.1	-1.4	0.0	yes
c. 962	128	0.1	0.1	0.0	0.0	no
c. 1078	133	4.9	0.2	4.7	3.6	yes
c. 1128	40	1.0	0.0	1.0	2.5	no
c. 1170	52	0.3	0.0	0.3	0.6	no
ct. 1251	93	11.3	6.2	5.2	5.5	yes
ct. 1410	128	2.7	2.4	0.3	0.2	yes
Averages	99	2.8	2.1	0.9	0.8	

*s = subclavian implant; c = carotid implant; ct = carotid transplant.

DISCUSSION

In the early part of our series, we did not appreciate the factor of bronchial flow. Arterial blood leaves the thoracic aorta through the bronchial arteries and, in part, enters the pulmonary circulation and traverses the pulmonary veins entering the left side of the heart. The bronchial flow is then ejected from the left ventricle into the aorta and the coronary ostia, returning through the coronary sinus to be measured by our right ventricular catheter. Although we believe that a stimulated bronchial collateral flow may well be a desirable feature of revascularization surgery, we feel that the data sought are confused by bronchial factors. For the past year and a half, we have been clamping the pulmonary hila which carry the bronchial inflow, thereby eliminating this factor from our results.

Analysis of the procedures of arterial implantations yielded only 3 animals with a flow in excess of the control levels. Nine animals showed only slight flow or no flow at all. Six of these 9 animals had patent implants at autopsy and demonstrated some degree of back bleeding during surgery. The patency of an implant does not ensure the fact that it provides increased flow to the myocardium. We have also demonstrated excellent filling of the coronary vascular tree by means of postmortem angiography through a patent arterial implant in a dog which had no increase in coronary flow following an arterial implantation. We do not believe that postmortem dye injection studies are adequate proof of functional success of revascularization operations (Figs 2 and 3).

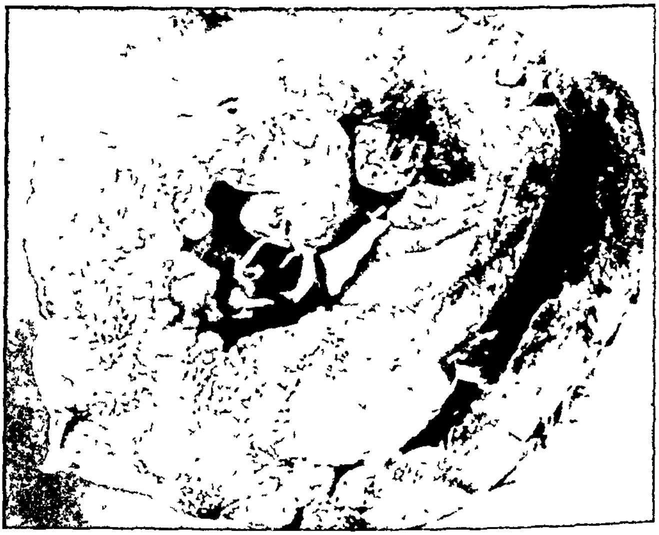

Fig 2.—Cross section of ventricle demonstrating a patent carotid artery implant.

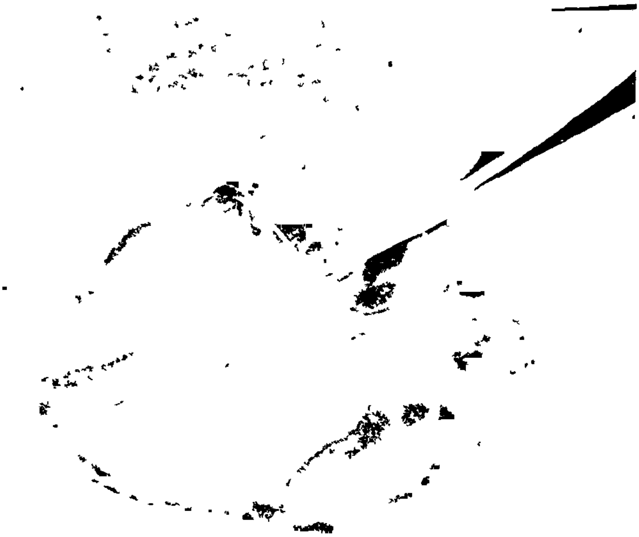

Fig 3—Dye injection study through patent carotid artery implant This implant did not increase the coronary flow

Following the use of talc and a chemical abrasive like phenol, or their combination, excellent adhesions were formed in every case. When the adhesions were stripped, a significant degree of vascularity was observed in some animals. In other animals the adhesions appeared avascular. We were unable to determine a relationship between the type of operation and vascularity of adhesions. The fact that there was a wide punctate ooze from the stripped adhesions did not ensure good flow, and adhesions observed as avascular were sometimes associated with excellent flow.

The clinical need for surgical revascularization of the heart results from a type of coronary insufficiency which is difficult to reproduce in the laboratory. Accordingly, we believe it is unwise to draw clinical conclusions on the basis of laboratory results in this area of study. With the knowledge that coronary ischemia acts as a stimulus to the development of coronary collateral flow,[8, 9] we propose to repeat some of these procedures for revascularization in animals whose hearts have been rendered ischemic by a method described by Pearl and his associates.[10]

SUMMARY

A 3-year study has been conducted in our laboratory to evaluate various procedures in clinical use to revascularize the heart. These procedures were the bilateral ligation of the internal mammary artery, the phenol-talc-lingula procedure, a phenol procedure, a talc procedure, and a lingula procedure, and subclavian and carotid arterial implantations.

Our method has been described previously and is briefly restated here.

Of the 8 animals with bilateral ligations of the internal mammary artery, 2 showed slight flow. There were seven phenol-talc-lingula operations and 4 of the animals had flow in excess of control levels. There were six lingula operations, and none of these animals showed significant flow. Seven animals underwent talc poudrage. Two of these 7 showed flow in excess of controls. Eight animals had phenol procedures and 3 had flow above control levels. In 13 animals, arterial implants were performed. Four of the 13 had subclavian implants and none of these had significant flow. Seven had carotid implants and only 2 of these had appreciable flow. Two had carotid transplants, and 1 had significant flow.

A patent implant does not necessarily indicate a functioning implant. The vascularity of adhesions is apparently unrelated to myocardial flow through the adhesions.

It is unwise to draw clinical conclusions from laboratory data in this area of experimentation.

REFERENCES

1. Thompson, S. A., and Plachta, A.: Fourteen Years' Experience With Cardiopexy in the Treatment of Coronary Artery Disease, J. THORACIC SURG. 27: 64, 1954.
2. Vineberg, A., and Miller, P.: Functional Evaluation of an Internal Mammary Coronary Artery Anastomosis, Am. Heart J. 45: 873-888, 1953.
3. Vineberg, A., Munro, D. D., Cohen, H., and Buller, W.: Four Years' Clinical Experience With Internal Mammary Implantation in the Treatment of Human Coronary Artery Insufficiency Including Additional Experimental Studies, J. THORACIC SURG. 29: 1, 1955.
4. Beck, C. S., and Hahn, R. S.: Revascularization of the Heart, Circulation 5: 801-809, 1952.

vascular tree by means of postmortem angiography through a patent arterial implant in a dog which had no increase in coronary flow following an arterial implantation. We do not believe that postmortem dye injection studies are adequate proof of functional success of revascularization operations (Figs. 2 and 3).

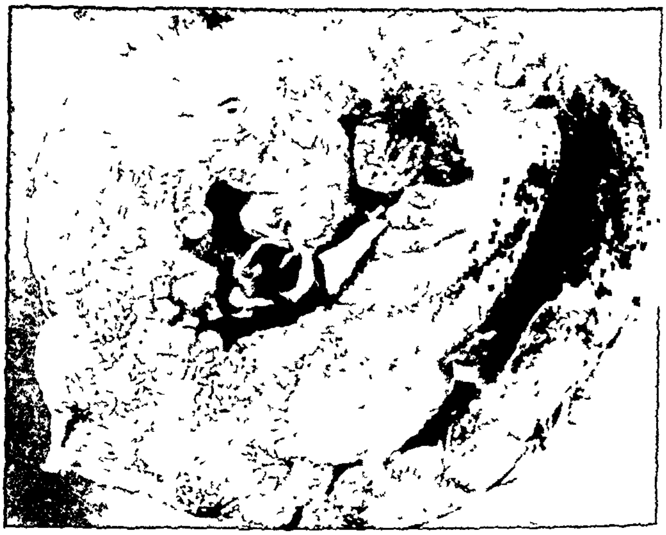

Fig. 2.—Cross section of ventricle demonstrating a patent carotid artery implant

Fig 3—Dye injection study through patent carotid artery implant This implant did not increase the coronary flow

Following the use of talc and a chemical abrasive like phenol, or their combination, excellent adhesions were formed in every case. When the adhesions were stripped, a significant degree of vascularity was observed in some

BRONCHIECTASIS

An Analysis of 240 Cases Treated by Pulmonary Resection

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INTRODUCTION

THIS REPORT is based on an analysis of 240 cases of bronchiectasis treated by pulmonary resection at Fitzsimons Army Hospital from January, 1947, to January, 1958. Cases of associated active tuberculosis or pulmonary tumors are excluded. This study deals with the symptomatology, some etiological factors, bacteriology, anatomic location, and distribution of the disease, surgical management, and analysis of results. Conclusions and some recommendations on this important pulmonary problem, as well as military aspects and facets, are discussed. Continuous periodic or limited follow-up has been successful in 92.5 per cent of the cases, and was obtained by annual letter questionnaires completed by patients, and progress reports from physicians, as well as subsequent clinical evaluation of many of the patients at this hospital.

The diagnosis was established preoperatively by bronchography. Until early in 1955, Lipiodol was employed as the contrast medium; during 1955 aqueous Dionosil was used and subsequently oily Dionosil has been employed and instilled under direct fluoroscopic visualization. Presently, we are of the opinion that oily Dionosil has all the advantages of Lipiodol and, in addition, disappears from view on the roentgenograms within a few hours after tracheobronchial instillation.[1]

Bronchoscopic findings were abnormal in 115 and normal in 67 of the 182 patients examined by this procedure. Most patients had various ventilatory function studies performed postoperatively; the majority had external spirometric determinations and, when considered indicated, internal spirometric studies were performed. The patients' ages ranged from 5 to 52 years, most patients being in their twenties.

CLINICAL MANIFESTATIONS

The most frequent complaint was a chronic or intermittent cough; this was usually productive of foul, purulent, or mucopurulent sputum, frequently yellow

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5. Battezatti, M., Tagliaferro, A., and deMarch, G.: Ligature of the Two Internal Mammary Arteries in the Vascular Disorders of the Myocardium, Minerva med. 46: 1178-1188, 1955.
6. Lord, J. W., Jr., Coryllos, E., Lowenfels, A., Dysart, R., Neumann, C., and Hinton, J. W.: Evaluation of Operations for Revascularization of the Myocardium by the Study of Coronary Blood Flow Using Extracorporeal Circulation, Surgery 43: 202-213, 1958.
7. DeWall, R. A., Warden, H. E., Read, R. C., Gott, V. L., Zeigler, N. R., Varco, R. L., and Lillehei, C. W.: A Simple Expendable Artificial Oxygenator for Open Heart Surgery, Surg. Clin. North America 36: 1025-1034, 1956.
8. Zoll, P. M., Wessler, S., and Schlesinger, M. J.: Interarterial Coronary Anastomosis in the Human Heart With Particular Reference to Anemia and Relative Cardiac Anoxia, Circulation 4: 797, 1951.
9. Von Wedel, J., Lord, J. W., Jr., Neumann, C. G., and Hinton, J. W.: Revascularization of the Heart by Pedicled Skin Flap, Surgery 37: 32-53, 1955.
10. Pearl, F.: Personal communications.

history of the disease. As reported in the literature, a history of associated chronic, paranasal sinusitis varies greatly in incidence.[6] This review indicates that only 12 of the 240 patients complained of having had chronic, paranasal sinusitis, although 27 were given treatment for such chronic infection during periods of hospitalization when pulmonary resections were performed. The past history in several cases gave very good evidence as to the causative event or agent; as for example, gunshot wound of chest, aspirations as a result of poliomyelitis or epilepsy, head injuries with unconsciousness, aspiration of a foreign body, and lung abscess.

PHYSICAL FINDINGS

A relatively common finding was the presence of moist râles in the area of bronchial disease; quite often such râles were demonstrated only on post-tussic auscultation. Râles and/or pleural friction rubs were found on approximately 75 per cent of patients. Clinical records revealed that 53 patients (22 per cent) had some degree of clubbing of fingers. Cor pulmonale was not evident by physical examination or on electrocardiographic evaluation prior to pulmonary resection in this series of patients.

Roentgenographic and Laboratory Findings.—All patients had bronchographic visualization of the tracheobronchial tree employing the three types of radiopaque media as mentioned previously. During the past 3 years, most patients have had bilateral stage bronchography performed, that is, the lung considered to be involved, or most markedly so, being evaluated first. This unilateral method largely obviates subsequent lateral and oblique roentgenograms in which the bronchi from both sides overlap, and thus reduces the possibility of misinterpretation of films. It has been our policy to ensure careful filling of every segment of each lobe in order that all pulmonary segments could be properly mapped and evaluated. Distribution of disease, as demonstrated by bronchography, is given in Table III.

TABLE III. LOBAR AND/OR SEGMENTAL DISTRIBUTION OF DISEASE AS DEMONSTRATED BY BRONCHOGRAPHY—240 CONSECUTIVE PATIENTS HAVING SURGICAL MANAGEMENT (RESECTIONS PERFORMED AS LISTED)

	INVOLVED	RESECTED
Right upper lobe	4	3
Right middle lobe	62	44
Superior segment right lower lobe	5	4
Right lower lobe and/or basilar segment	67	51
Left upper lobe equivalent	5	3
Lingula	85	71
Superior segment left lower lobe	6	4
Left lower lobe and/or basilar segment	151	136
Residual disease, unduly long left lower lobe bronchial stump plus ectasia lingula	2	2
Total lobes and/or segments*	407	318

*Total pneumonectomy was performed on 2 patients—one for extensive unilateral disease on the left side; the other after technical problems arose during surgical dissection on the right side. Demonstrable disease by bronchography remained in 59 lobes and/or segments in 55 patients after pulmonary resection.

or lime green in color, and ranged in volume from 8 to 500 ml. per day. Chest pain was rarely severe; it was commonly described as a heavy, dull ache on the side which subsequently proved to be the site of the most markedly involved pulmonary segments or lobes; quite frequently, the discomfort was pleuritic in type. Massive hemoptysis was described or observed in 12 patients, 4 of whom required blood transfusions; "streaking" was a rather frequent complaint. Twelve patients (5 per cent) were asymptomatic. A comparison is made with Ogilvie's series of 68 patients reported in 1941—all of whom were symptomatic.[2] In this asymptomatic group, diagnoses were established after suggestive clues were found in routine roentgenograms; generally, such abnormalities proved to be collapse of lobes or segments and, frequently, emphysema as the result of long-standing disease. Dyspnea was a clinically significant complaint in 20 of 28 patients who had this symptom; it was not possible to correlate the subjective complaint of exertional dyspnea and the severity and extent of the disease as demonstrated on bronchography. We continue to be of the opinion, as previously reported, that dyspnea is usually a late symptom.[3] Twelve patients entered with the symptoms of acute, respiratory infection.

TABLE I. PREDOMINANT SYMPTOMS IN 240 PATIENTS HAVING PULMONARY RESECTION

	NUMBER OF PATIENTS
Productive cough	201
Hemoptysis and/or streaking	65
Chest pain	54
Weight loss	40
Exertional dyspnea	28
Cough (seldom productive)	14
Undue fatigue	12
Chills and fever	12
No symptoms (abnormality noted on routine roentgenogram)	12
Hoarseness	1

As observed by others, more than one half, 148 patients, had a history of previous pneumonia.[4, 5] We believe that bronchopneumonia frequently is etiological in bronchial ectasia, associated with chronic suppuration and pulmonary fibrosis. Recurring episodes of pneumonia were often reported and observed clinically and should be considered, although less frequently than prior to the antibiotic era, as a rather typical sequence, in conformity with the natural

TABLE II. PERTINENT PAST HISTORY, 240 PATIENTS

	NUMBER OF PATIENTS
Previous and/or recurrent pneumonia	148
Negative past history	46
Pertussis	30
Sinusitis	12
Previous empyema	9
Tuberculosis, previous	5
Gunshot wound of chest	4
Asthma	4
Head injury with unconsciousness	2
Poliomyelitis, in respirator	1
Epilepsy with convulsions	1
Foreign body	1
Lung abscess	1

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Bacteriologic study in this series of patients was far from complete. The results of cultures from bronchial secretions are listed in Table IV. Most material for identification of predominant organisms was obtained by bronchial aspiration during endoscopic examination.

TABLE IV. BACTERIOLOGY ON BRONCHIAL ASPIRATES*

	NUMBER OF PATIENTS
Not studied or reported	132
Streptococcus viridans	49
Hemolytic streptococcus	44
Neisseria catarrhalis	36
Aerobacter aerogenes	24
Pseudomonas aeruginosa	19
Pneumococcus	8
Beta hemolytic streptococcus	8
Staphylococcus aureus	3
Escherichia coli	3
Nonhemolytic streptococcus	2
Friedlander's bacillus	1

*Quite often two and rarely three specific organisms were cultured from a bronchial specimen.

SURGICAL ASPECTS

Of the 240 patients having pulmonary resection for bronchiectasis during the 11-year period, all but 18 have been followed for periods ranging from 1 year to 10 years and 9 months. The average follow-up period after pulmonary resection was 4 years and 10 months. The involved lobes and segments removed are listed along with remaining involved anatomic pulmonary components in Table III. The lingula and left lower lobe were found to be most frequently involved as has been recorded by most investigators who have reported on the anatomic distribution of this disease. Of the 157 patients having ectasia involving the left lower lobe, 85, or 54 per cent, had demonstrable involvement in one or both divisions of the lingula. This finding is in contrast to the identifiable bronchographic disease on the right where the lower lobe was involved in 72 patients and one or both segments of the middle lobe was ectatic in 62 patients. Not infrequently the middle lobe was the site of disease when none could be demonstrated in the right lower lobe. Conversely, we found a diversity in comparable anatomic locations, in that the lingula was seldom involved without some bronchiectasis of one or more segments of the left lower lobe; localized left bronchographic disease limited only to the lingula was demonstrated in only 3 patients and 1 of these had contralateral involvement of the middle lobe.

The predominance of combined left lower lobar and lingular segmental resections over similar operations on the right lung is noteworthy. Partial or total lingulectomy was combined with complete left lower lobectomy or resection of the basilar segments in 77 patients, whereas simultaneous total middle and right lower lobectomies were performed only 21 times. Lobectomy was done exclusively early in the series. In the interest of conserving normal bronchopulmonary units and pulmonary function, segmental resection has been the procedure of choice, when applicable, since early in 1954. The technique of mass hilar ligation was never employed, and in all cases anatomic dissection of the bronchovascular structures was done. Two patients had bilateral staged resections, and 3 had repeat resections on the left—2 of these had had initial surgery elsewhere, and 1 at this hospital, 1 having completion of left lower lobectomy, and the other 2 had lingulectomy performed along with removal of elongated and widened left lower lobe bronchial stumps. Bilateral procedures were uncommon as extensive bilateral disease is relatively rare in service personnel, and, when seen, the patient is not considered a likely candidate to return to duty with troops after having bilateral pulmonary resection. There were 185 patients who had all apparent bronchiectatic disease removed, and 55 who had diffuse or bilateral disease remaining after the most extensively involved segments or lobes were resected. During the last 2 years of this study only 26 resections were performed and, of these patients, 22 had, on bronchographic study, unilateral, localized disease. The policy of curtailing pulmonary resection for bronchiectasis resulted after it was ascertained that many service personnel were not measurably benefited or would not admit improvement after resection therapy.[3, 7, 8, 9]

Postoperative Complications.—Complications which occurred in the 240 patients having 243 primary resections are given in Table V. There were no postoperative complications in 77 per cent of the patients. The most frequent postoperative difficulty was atelectasis. The relatively low complication rate, we feel, reflects the value of effective antibiotics, improved anesthetic techniques, adequate blood replacement during and following surgery, and detailed postoperative care. Table VI lists the methods of treatment employed for the surgical complications. Of the sixty-one surgical measures considered essential in

TABLE V. POSTOPERATIVE COMPLICATIONS

	NUMBER OF PATIENTS
None	187
Atelectasis*	27
Temporary pleural space problems	15
Bronchopleural fistula	11
Empyema	5
Hemothorax	5
Postoperative psychosis	2
Retention surgical sponge	1
Deaths	2

*Some patients had more than one complication.

TABLE VI. METHODS OF MANAGEMENT OF COMPLICATIONS

		NUMBER OF PATIENTS
Bronchoscopy		20
Re-insertion of pleural drainage tubes		14
Thoracoplasty		7
Open pleural drainage		7
Secondary thoracotomy		4
For control of bleeding	3	
For removal of sponge	1	
Tracheostomy		4
Pleural instillation streptokinase-streptodornase (Varidase)		3
Muscleplasty		2

the management of the complications, only thirteen are considered to be major; these being thoracoplasty, secondary thoracotomy, and muscleplasty procedures. The fact that there were eleven bronchopleural fistulas, and only five empyemas may to some extent reflect the value of appropriate antibiotics.

There were two postoperative deaths. A 25-year-old male developed lower nephron nephrosis following a difficult and prolonged pulmonary resection; death occurred on the ninth postoperative day. The second death in a 29-year-old male was attributed to massive pulmonary embolism on the third postoperative day.

SURGICAL RESULTS

Of the 220 patients followed from 1 year to 10 years and 9 months (2 patients died early in the postoperative period, and 18 were lost to follow-up), surgical results have been classified as excellent, improved, unchanged, and poor. The information requested or obtained in periodic questionnaires, or at clinical evaluation, was directed to ascertain whether there was a productive cough, frequent pulmonary infections, chest pain, hemoptysis, ability to work—if so, hours per day, and if a change in symptoms had occurred when compared with the preoperative state. Patients were encouraged to make additional statements in regard to their general health. Those classified as obtaining an *excellent* result were completely free of any symptoms suggestive of bronchiectasis, and considered themselves cured. Those considered *improved* have had some relief of symptoms but still had some chronic pulmonary complaints. Patients placed in the *unchanged* group have not had symptoms significantly altered, and in the *poor* results category we have listed those who are worse off since surgical resection and the clinical story is essentially that of the natural history of the disease as exemplified prior to the antibiotic era.

The results were considered from several standpoints. First the over-all results, the modification of the disease in service personnel, and the results in dependents of military personnel—most of these being wives. We believe that this latter group of patients would more nearly reflect the results to be expected in civilian patients as this group had nothing to gain from a financial standpoint by exaggerating their postoperative complaints.

TABLE VII. RESULTS OF PULMONARY RESECTION IN 220 PATIENTS (157 MILITARY AND 63 DEPENDENTS) FOLLOWED 1 TO 10 YEARS AND 9 MONTHS (AVERAGE FOLLOW-UP 4 YEARS AND 10 MONTHS)

	EXCELLENT		IMPROVED		UNCHANGED		POOR		DEAD	
	NO.	PER-CENT	NO.	PER-CENT	NO.	PER-CENT	NO.	PER-CENT	NO.	PER-CENT
Military	25	15.9	45	28.7	74	47.1	9	5.8	4	2.54
Dependents	24	38	28	44.4	9	14.4	1	1.6	1	1.6
All cases	49	22.2	73	33.2	83	37.7	10	4.5	5	2.27

The results are tabulated on patients having postoperative complications (Table VIII), and the results when all apparent bronchiectatic disease was removed, as well as when known bronchographic bronchiectasis remained after pulmonary resection (Tables VIII and IX).

TABLE VIII. RESULTS FOLLOWING SURGICAL COMPLICATIONS

31 PATIENTS HAVING SURGICAL COMPLICATIONS (MAJOR)		22 PATIENTS HAVING SURGICAL COMPLICATIONS (MINOR)	
Excellent	3	Excellent	5
Improved	6	Improved	9 (41%)
Unchanged	13 (42%)	Unchanged	7
Poor	3	Poor	0
		Not followed	1
Deaths:			
Postoperative	2		
pulmonary embolism			
lower nephron nephrosis			
Late	2		
suicide			
cor pulmonale			
Not followed	2		

TABLE IX. RESULTS IN 185 PATIENTS HAVING ALL DEMONSTRABLE DISEASE REMOVED

Excellent	46 (25%)
Improved	60 (32%)
Unchanged	57 (31%)
Poor	5
Deaths	
Both postoperative	2
pulmonary embolism	
lower nephron nephrosis	
Not followed	15

The over-all results were not as good as had been expected inasmuch as 42 per cent of the patients followed do not admit or feel that their symptoms were improved following pulmonary resection. The known mortality rate to date is slightly over 3 per cent in 222 patients followed; 220 having been followed for an average period of 4 years and 10 months. Two patients died early in the postoperative period. Five patients died from 1 to 8 years after initial surgical intervention; causes of death are listed in Table X.

TABLE X. RESULTS IN 55 PATIENTS WHO DID NOT HAVE ALL BRONCHOGRAPHIC DISEASE REMOVED

Excellent	3
Improved	13
Unchanged	26 (47%)
Poor	5 (Living)
Deaths	5
Suicide—had extensive bilateral residual disease	
Coronary thrombosis	
Cor pulmonale	
Myocardial failure 24 hours following subsequent resection elsewhere	
Glomerulonephritis following subsequent resection elsewhere	
Not followed	3

During 1956 and 1957, it was our intended policy to offer surgery only to those patients who were demonstrated to have unilateral and localized ectatic disease. Of the 26 patients who had resections during this period, 22 had all demonstrable disease removed. In the group having resection of all bronchiectatic disease, 8 were military patients and 14 wives or other dependents of servicemen. Of the 8 military patients, 6 have indicated that they were *improved* and 2 do not feel that their symptoms have been altered after pulmonary resection and their disease is categorized as being *unchanged.* None will admit that symptoms have been altered sufficiently to classify the procedure as having given excellent results. Of the 14 dependent patients (mostly wives), 6 (43 per cent) have what appear to be *excellent* results and the remaining 8 feel that their symptoms have been quite measurably *improved.* Of the 4 patients in whom not all demonstrable disease was removed, during 1956-1957, only 1 civilian dependent admits that she is improved. The remaining 3 consider their symptoms unchanged—1 being a 23-year-old female who had a thoracotomy on the left side with removal of an elongated bronchiectatic lower lobe stump and lingulectomy for cylindrical disease 5 years after a left lower lobectomy performed elsewhere. No technical difficulty was encountered during the secondary thoracotomy and recovery from the procedure was relatively uneventful; however, her symptoms have not been altered significantly.

Pathologically most cases in this study were diagnosed as and proved to be nonspecific bronchiectasis of varying degrees of severity. Table XI lists associated and/or incidental pathologic processes detected in the pulmonary surgical specimens. In only one specimen was a foreign body considered to be an etiological factor; this proved to be a cocklebur in a lower lobe bronchus.

TABLE XI. SPECIFIC AND/OR UNSUSPECTED PATHOLOGY

	CASES
Middle lobe syndrome, etiology unknown	5
Middle lobe syndrome, due to histoplasmosis	3
Granuloma, etiology unknown	2
Coccidioidomycosis	1
Lipoid pneumonia	1
Eosinophilic granuloma	1
Foreign body	1

DISCUSSIONS AND CONCLUSIONS

This follow-up study and evaluation of 220 patients who have had pulmonary resection for bronchiectasis (157 military and 63 civilian dependents) presents rather conclusive evidence that poor or questionable surgical results may be anticipated when only the most markedly involved segments or lobes of widespread unilateral or bilateral bronchiectatic disease are removed. This contention and firm clinical impression are offered, even though our series of patients has been weighted heavily on the military side. Perhaps, it is noteworthy that 106 of 185 patients, 57 per cent, having had all demonstrable ectatic disease resected, admitted that they had obtained excellent results or had been improved after surgical management; however, only 29 per cent of the 55 not having all disease removed were of the opinion that their chronic disease had been favorably altered—of these only 3 (5.4 per cent) admitted complete relief of symptoms. In view of clinical impressions gleaned long before the completion of this study, we have taken a "new look" at the problems of bronchiectasis in both military personnel and their civilian dependents and have modified our former concepts on the indications for surgical management of this chronic pulmonary disease rather significantly. This study, which is a continuation of a former survey, continues to reveal that over-all surgical results are approximately twice as good in civilian dependents as in military patients.[3] Such results reflect to some degree factors which cannot be accurately assessed, such as the influence of possible financial gain in the form of disability remuneration and poor motivation regarding continuation of service or future geographic duty assignments.

For the past 3 years our "surgical philosophy" and essential policy in regard to bronchiectasis follows.

1. Military personnel having relatively short periods of service and localized or multilobar bronchiectasis are processed for discharge from the service prior to recommendations for or any form of pulmonary resection.

2. Serious episodes of bleeding or extension of the bronchial and parenchymal infection into the pleura may make surgical intervention mandatory; these complications have been extremely uncommon in recent years.

3. Personnel with long periods of service (over 8 years), who have symptomatic bronchiectasis should, after proper clinical evaluation and medical management, be considered for definitive surgical care.

4. Patients with bilateral disease, especially if the cylindrical type, should seldom, if ever, have surgical resections for the following reasons: (a) such patients seldom have sufficient ventilatory reserve to allow for staged excision of all involved segments, and (b) cylindrical disease is prone to be progressive, regardless of the type of management. Some of us postulate that this form of diffuse bilateral disease may be related to hereditary influences. Some other patients show generalized narrowing of terminal bronchi and bronchioles—a superimposed generalized bronchiolitis. Our experience with such complex problems has been sufficient for us to make the categorical statement that such patients often have serious postoperative complications and only rarely are their symptoms appreciably relieved following surgery.

5. Secondary thoracotomy for removal of residual ectatic segments, lobes, and/or unduly long residual bronchial stumps, under most circumstances, is not recommended; this somewhat dogmatic principle and policy even approaches a "dictum" when there is bronchographic evidence of contralateral disease.

SUMMARY

A critical review of 240 cases of bronchiectasis treated by pulmonary resection from January, 1947, to January, 1959, is presented and follow-up results tabulated. Trends regarding the over-all problem and our changing concepts and philosophy in the surgical management of this chronic pulmonary disease are briefly discussed. Our present policy of hesitancy to perform pulmonary resection on young soldiers with short periods of active service, who experienced

serious pulmonary symptoms prior to induction, resulted after preliminary follow-up studies were evaluated 3 years before completion of this study. The low salvage rate of those able to perform effective military service has made it seem administratively and professionally prudent to adopt this restrictive surgical policy. Long-term results after pulmonary resection in civilian dependents have been approximately twice as favorable when compared with the surgical results in military personnel.

We continue to recommend pulmonary resection to patients who have bronchiectasis incurred or aggravated during military service; however, such patients should have the type of localized disease which can be expected to be benefited significantly by surgical extirpation.

REFERENCES

1. Wisoff, C. P., and Felson, B.: Bronchography With Oily Dionosil, J. THORACIC SURG. 29: 435, 1955.
2. Ogilvie, A. G.: The Natural History of Bronchiectasis; A Clinical Roentgenologic and Pathologic Study, Arch. Int. Med. 68: 395, 1941.
3. Taylor, R. R., and Salyer, J. M.: Bronchiectasis and the Military Service. Eleventh Annual Symposium on Pulmonary Disease, Fitzsimons Army Hospital, Lecture No. 8: 97, 1958.
4. Ochsner, A., De Bakey, M., and DeCamp, P. T.: Bronchiectasis: Its Curative Treatment by Pulmonary Resection: An Analysis of 96 Cases, Surgery 25: 518, 1949.
5. Kay, E. B.: Bronchiectasis Following Atypical Pneumonia. Arch. Int. Med. 75: 89, 1945.
6. Riggins, H. M.: Present Concepts of Pathogenesis, Morbidity, Mortality and Treatment of Bronchiectasis, Dis. Chest 9: 5, 1943.
7. Harris, H. W.: Personal communication.
8. Pinney, C. T.: Personal communication.
9. Gregory, L. J.: Personal communication.

MESOTHELIOMAS OF THE PLEURA

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THE morphology and cytology of primary pleural tumors have been in dispute for many years. There are some who even now deny the existence of these neoplasms.[19] Robertson,[14] in 1924, published an extensive historic review on this subject and pointed out the confusion which existed in the classification and nomenclature at that time. It was his opinion, based on his own experience, that there is no definite entity of pleural endotheliomas. He believed that only sarcomas can be classified as primary malignant tumors of the pleural tissue and that all other growths are secondary, representing extensions, implantations, or metastases from unrecognized or latent primary sources, usually the lungs. Maximow,[12] in 1927, was able to grow colonies of fibroblasts in mesothelial tissue cultures. Some of the cells showed epithelial characteristics but finally all acquired fibroblastic characteristics. Klemperer and Rabin,[11] in 1931, reviewed the literature and brought some order out of chaos by introducing a classification which is essentially the one used today. They recognized localized pleural tumors which they believed to arise from tissues beneath the pleura itself. These tumors show a great variation of cell type and are of varied degrees of malignancy. They are usually described as sarcomas or subgroups thereof. The diffuse pleural neoplasms Klemperer and Rabin believed to arise from the surface lining cells. They are malignant and contain a mixture of epithelial and mesothelial cells. Clagett[3] agreed with Robertson as to the origin of the two types of neoplasms. He suggested the classification of localized fibrous mesotheliomas and diffuse malignant mesotheliomas. However, Stout and Murray,[16] in 1942, were able by tissue culture to clarify the mesothelial origin of pleural tumors. Sano,[15] in 1950, working with tissue from a diffuse mesothelioma, was able to demonstrate the presence of epithelial-like cells in tissue cultures even though they were not seen in histologic sections obtained from the neoplasm.

The pleural lining cells theoretically may have the potentiality to form epithelial and fibroblastic cell types. The pleura is derived embryologically from the middle germ layer, the mesoderm, which arises from ecto- and entodermal layers. The mesoderm splits into two lamellae, one fusing with the

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ectoderm forming the somatopleura, the other with the entoderm forming the splanchnopleura. The visceral mesoderm gives rise to the cellular lining of the serosal surfaces which are the site of the neoplasms under discussion.

Endothelial pleural surfaces on the other hand are known to show morphologic changes resembling epithelial cells when subjected to irritation.

Stout and Himadi,[17] in 1951, published a report of 8 cases of localized mesotheliomas which were surgically treated. They were classified as solitary fibrous mesotheliomas and it was pointed out that even though these lesions may be of low grade malignancy they are sharply circumscribed and are curable by surgical excision.

Essentially there seem to be two groups of pleural neoplasms. One is the diffuse type which is highly malignant and usually rapidly fatal. The characteristics are the presence of epithelial cells in tubular or glandular arrangements mixed with sarcomatous neoplastic cells. The localized type contains fibrous tissue elements only and may show great variation in cell morphology. They may be benign or show all degrees of malignancy. Yesner and Hurwitz[21] have reported a case of a localized pleural mesothelioma of the epithelial type which was resectable. Bogardus[2] describes a localized malignant mesothelioma with pleural implants. It stands to reason that diffuse epithelial mesotheliomas arise in a localized area and that they could be treated surgically if they are found and diagnosed before extensive pleural spread has taken place. After the entire pleural space has been involved by spreading and implanting tumor, it is often impossible to determine where the original site of the pleural neoplasm has been.

Pleural mesotheliomas have been recognized with increasing frequency and many have been reported in the recent literature.[6, 8, 9, 10, 13, 18, 20] Nevertheless, they are rare neoplasms. The correct diagnosis is often not made in the diffuse spreading, highly malignant type until just before or after death of the patient. The localized fibrous, benign, or malignant types may produce no symptoms and may be accidental findings during routine chest survey studies. Some of the symptoms seem to be entirely unrelated to the intrathoracic lesion. Osteoarthropathy, chills, and fever may be the main complaints and the pulmonary lesion may escape early correct detection. Furthermore, the roentgenologic appearance of these lesions is not at all diagnostic. The often massive bloody pleural effusions which are nearly always present in patients with diffuse malignant mesothelioma may also be seen with benign well-localized pleural lesions. Cytologic studies of the pleural fluid have been of no help in our experience. Endoscopic examinations and bronchography have not helped except to demonstrate displacement of intrathoracic structures by very large masses. The large localized tumors produce symptoms and signs only by compression and displacement of the adjacent organs without actually involving them.

Exploratory thoracotomy with either resection of localized tumors or biopsy in the nonresectable group is the only reliable method to arrive at a diagnosis.

We have collected a total of 16 patients treated in the Surgical Department, University of Iowa Hospitals. The earliest documented and correctly diagnosed patient was seen in 1927. It is difficult to group the cases into either the diffuse or localized varieties. On the basis of cell types and the clinical appearance, we placed 8 patients in the group of localized pleural mesotheliomas and the rest in the group of diffuse malignant mesotheliomas. All other possible cases in which there were doubtful diagnoses or a history of previous extrathoracic neoplastic disease were excluded.

CASE REPORTS

Table I. Localized Fibrous Mesothelioma

CASE NO	AGE AND SEX	DURATION OF SYMPTOMS	TIME LESION WAS KNOWN	DATE OF OPERATION	RESULT
1	25 F	8 mo.	8 mo.	11/23/27 Resection of tumor	Emypema; death 5 mo. after diagnosis
2	30 M	None	2½ mo.	8/17/51 Right lower lobectomy and resection of tumor	Alive
3	25 F	2 yr.	Recurrent lesion, 2 mo.	11/5/53 Resection of tumor	Alive
4	57 M	?	1 yr.	2/22/55 Right lower lobectomy and resection of tumor	Alive
5	68 F	5 mo.	7 yr.	3/4/55 Resection of tumor	Alive
6	53 M	5 mo.	1 mo.	3/8/55 Resection of tumor	Alive
7	77 F	3 yr.	?	5/20/55 Pneumonectomy	Metastases to chest wall July, 1959
8	69 M	4 mo.	1 mo.	9/5/57 Resection of tumor	Alive

Case 1.—G. J. (B 10311), a 25 year-old woman, was admitted on Nov. 20, 1927. Entrance complaints were fatigue and chest pain with coughing for 8 months. She also developed temperature elevations up to 102° F. during this time. There had been no weight loss. At the time of admission, a large globular tumor located in the lower right side of the chest was found. On Nov. 23, 1927, a right thoracotomy was carried out. A well encapsulated tumor was found in the interlobar space between the upper, middle, and lower lobes. The tumor was resected. The mass measured 11 by 9 by 12 cm. and weighed 140 grams. It had a grayish, granular appearance with many papillary cauliflower-like projections. Sections revealed a very cellular neoplasm of fibroblastic nature with many mitotic figures. The impression was that it was a pleural fibrosarcoma. This patient had a stormy postoperative course and succumbed to a postoperative empyema on April 22, 1928.

Case 2.—D. M. (51 9301) (Figs. 1, *A*, *B*, and *C*). A 30 year old male farmer was admitted on Aug. 14, 1951, with the complaint of a tumor in the right lung known for 2½ months. The patient had no symptoms. The lesion was found during routine chest survey studies. Roentgenograms showed a right posterior mediastinal mass, possibly representing a lung cyst or neurofibroma. Bronchograms and esophagrams demonstrated displacement of the lower esophagus to the left and displacement of the right main bronchus by the large mass. On Aug. 17, 1951, a right lower lobectomy and resection of the large tumor was carried out. The pathologic report stated it was inflammatory pseudotumor of pleura.

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Endothelial pleural surfaces on the other hand are known to show morphologic changes resembling epithelial cells when subjected to irritation.

Stout and Himadi,[17] in 1951, published a report of 8 cases of localized mesotheliomas which were surgically treated. They were classified as solitary fibrous mesotheliomas and it was pointed out that even though these lesions may be of low grade malignancy they are sharply circumscribed and are curable by surgical excision.

Essentially there seem to be two groups of pleural neoplasms. One is the diffuse type which is highly malignant and usually rapidly fatal. The characteristics are the presence of epithelial cells in tubular or glandular arrangements mixed with sarcomatous neoplastic cells. The localized type contains fibrous tissue elements only and may show great variation in cell morphology. They may be benign or show all degrees of malignancy. Yesner and Hurwitz[21] have reported a case of a localized pleural mesothelioma of the epithelial type which was resectable. Bogardus[2] describes a localized malignant mesothelioma with pleural implants. It stands to reason that diffuse epithelial mesotheliomas arise in a localized area and that they could be treated surgically if they are found and diagnosed before extensive pleural spread has taken place. After the entire pleural space has been involved by spreading and implanting tumor, it is often impossible to determine where the original site of the pleural neoplasm has been.

Pleural mesotheliomas have been recognized with increasing frequency and many have been reported in the recent literature.[6, 8, 9, 10, 13, 18, 20] Nevertheless, they are rare neoplasms. The correct diagnosis is often not made in the diffuse spreading, highly malignant type until just before or after death of the patient. The localized fibrous, benign, or malignant types may produce no symptoms and may be accidental findings during routine chest survey studies. Some of the symptoms seem to be entirely unrelated to the intrathoracic lesion. Osteoarthropathy, chills, and fever may be the main complaints and the pulmonary lesion may escape early correct detection. Furthermore, the roentgenologic appearance of these lesions is not at all diagnostic. The often massive bloody pleural effusions which are nearly always present in patients with diffuse malignant mesothelioma may also be seen with benign well-localized pleural lesions. Cytologic studies of the pleural fluid have been of no help in our experience. Endoscopic examinations and bronchography have not helped except to demonstrate displacement of intrathoracic structures by very large masses. The large localized tumors produce symptoms and signs only by compression and displacement of the adjacent organs without actually involving them.

Exploratory thoracotomy with either resection of localized tumors or biopsy in the nonresectable group is the only reliable method to arrive at a diagnosis.

We have collected a total of 16 patients treated in the Surgical Department, University of Iowa Hospitals. The earliest documented and correctly diagnosed patient was seen in 1927. It is difficult to group the cases into either the diffuse or localized varieties On the basis of cell types and the clinical appearance, we placed 8 patients in the group of localized pleural mesotheliomas and the rest in the group of diffuse malignant mesotheliomas. All other possible cases in which there were doubtful diagnoses or a history of previous extrathoracic neoplastic disease were excluded.

CASE REPORTS

TABLE I. LOCALIZED FIBROUS MESOTHELIOMA

CASE NO	AGE AND SEX	DURATION OF SYMPTOMS	TIME LESION WAS KNOWN	DATE OF OPERATION	RESULT
1	25 F	8 mo.	8 mo.	11/23/27 Resection of tumor	Emypema; death 5 mo. after diagnosis
2	30 M	None	2½ mo	8/17/51 Right lower lobectomy and resection of tumor	Alive
3	25 F	2 yr.	Recurrent lesion, 2 mo.	11/5/53 Resection of tumor	Alive
4	57 M	?	1 yr.	2/22/55 Right lower lobectomy and resection of tumor	Alive
5	68 F	5 mo.	7 yr.	3/4/55 Resection of tumor	Alive
6	53 M	5 mo.	1 mo.	3/8/55 Resection of tumor	Alive
7	77 F	3 yr.	?	5/20/55 Pneumonectomy	Metastases to chest wall July, 1959
8	69 M	4 mo	1 mo	9/5/57 Resection of tumor	Alive

CASE 1.—G. J. (B 10311), a 25 year-old woman, was admitted on Nov. 20, 1927. Entrance complaints were fatigue and chest pain with coughing for 8 months. She also developed temperature elevations up to 102° F. during this time. There had been no weight loss At the time of admission, a large globular tumor located in the lower right side of the chest was found. On Nov. 23, 1927, a right thoracotomy was carried out. A well encapsulated tumor was found in the interlobar space between the upper, middle, and lower lobes The tumor was resected. The mass measured 11 by 9 by 12 cm. and weighed 140 grams. It had a grayish, granular appearance with many papillary cauliflower like projections. Sections revealed a very cellular neoplasm of fibroblastic nature with many mitotic figures The impression was that it was a pleural fibrosarcoma. This patient had a stormy postoperative course and succumbed to a postoperative empyema on April 22, 1928

CASE 2.—D. M. (51 9301) (Figs 1, *A*, *B*, and *C*). A 30 year old male farmer was admitted on Aug. 14, 1951, with the complaint of a tumor in the right lung known for 2½ months The patient had no symptoms The lesion was found during routine chest survey studies. Roentgenograms showed a right posterior mediastinal mass, possibly representing a lung cyst or neurofibroma. Bronchograms and esophagrams demonstrated displacement of the lower esophagus to the left and displacement of the right main bronchus by the large mass. On Aug 17, 1951, a right lower lobectomy and resection of the large tumor was carried out The pathologic report stated it was inflammatory pseudotumor of pleura.

The mass measured 18 by 15 by 10 cm. Microscopic section showed fibrous interlacing connective tissue tumor. In areas the structures had a myxomatous appearance. The postoperative course was uneventful. The patient is alive.

CASE 3.—D. A. (53-12248), a 25-year-old woman, was admitted on Nov. 2, 1953 (Figs. 2, *A* and 2, *B*). A benign mesothelioma of the pleura had been removed at the Mayo Clinic on Oct. 5, 1951. She stated that her symptoms before that time were afternoon temperature elevations and fatigue. The last follow-up roentgenogram in May, 1952, was normal. A roentgenogram on Sept. 4, 1953, revealed recurrence of a sharply circumscribed 2 cm. mass in the left lower lung field. The patient again had temperature elevations in the afternoon up to 101° F. The mass was excised on Nov. 5, 1953. The pathologic report stated it was fibroblastic tumor within lung parenchyma consistent with mesothelioma. This lesion was contained within the anterior basilar segments of the left lower lobe. The patient has been well since.

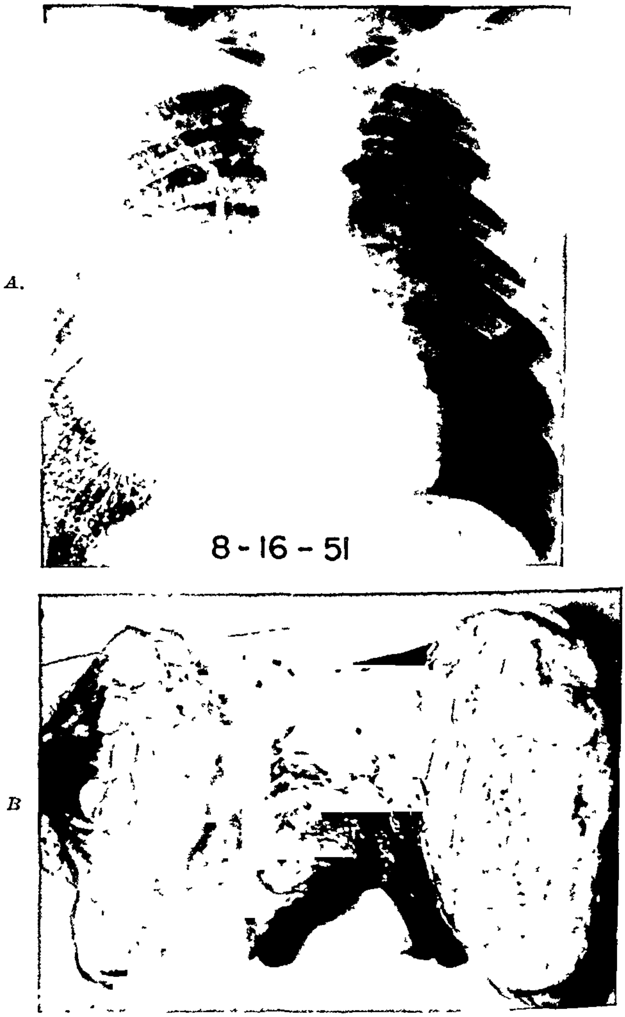


Fig. 1.—Case 2. *A*, Bronchogram which shows the large mass in the right hemithorax. *B*, Cross section through specimen which shows the well-encapsulated lobulated tumor and uninvolved attached right lower lobe.

Case 4.—S. P. (54-12270), a 57-year-old man, was admitted on Feb. 20, 1955, complaining of cough. A roentgenogram revealed what was thought to be an elevated right leaf of the diaphragm. On further investigation a large posterior rounded encapsulated mass in the right supradiaphragmatic area was found. On Feb. 22, 1955, at right thoracotomy, a right lower lobectomy and resection of a large mass, measuring 15 cm. in diameter and lying between the right lower lobe and the diaphragm. was carried out. The mass weighed 650 grams. The microscopic report stated it was fibroma of pleura with probable low grade sarcomatous changes. The right lower lobe showed only collapse and fibrosis. The postoperative course was uneventful. The patient is alive and well.

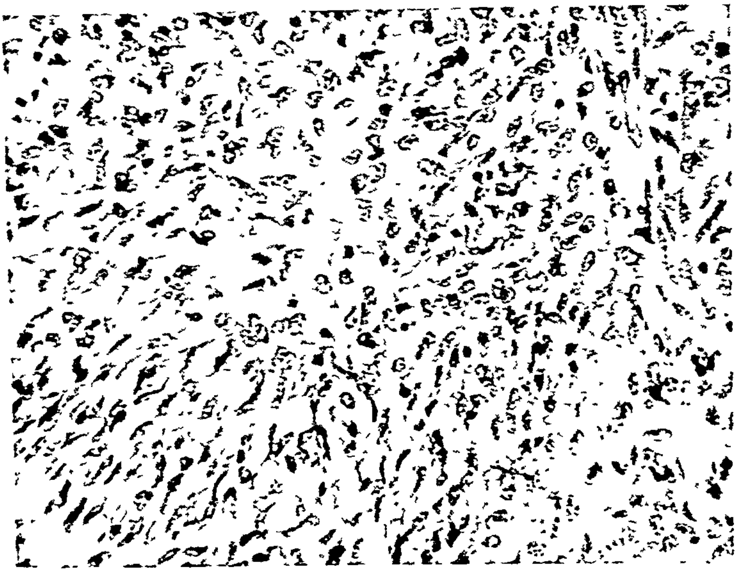


Fig. 1—Cont'd C, Microscopic section: Myxomatous interlacing fibroblastic tissue without evidence of malignant change.

Case 5.—K. S. (55-2160), a 68-year-old woman. was first seen Feb. 15, 1955 (Fig. 3). A history was obtained of a lesion in the left lung field first seen in roentgenograms taken during 1948. Nothing was done at that time. The entrance complaint was severe shortness of breath and some neuralgic pain in both hands for 5 months. Roentgenograms revealed a massive left pleural effusion with mediastinal shift to the right. On thoracentesis, a hemothorax was found. The fluid failed to show abnormal cells. On March 4, 1955, a left thoracotomy revealed a large mass located in the fissure between the upper and lower lobes, partly attached to the chest wall. This lesion was removed. There were no pleural implants. The pathologic report stated it was cellular fibroma or very low grade fibrosarcoma. The patient made an uneventful postoperative recovery and she is alive with no further symptoms.

Case 6.—A. B. (55-3602), a 53-year-old college professor. was admitted on March 21. 1955. He complained of shortness of breath for the previous 5 months. Roentgenograms taken shortly after admission revealed a large mass in the right upper lung field. Bronchoscopy and bronchograms showed the mass to displace the pulmonary tissue. On March 28, 1955, a right thoracotomy was done. An encapsulated tumor was encountered. lying within the pleural space and compressing lung, having attached itself to portions of the upper and middle lobes but not invading those structures. The mass was resected. The specimen weighed 1,300 grams. On cross section it had a nodular appearance and was well encapsulated. The pathologic report stated it was pleural sarcoma with considerable pleomorphism of the cellular structures. There was some mitotic activity. The patient is alive and well.

Case 7.—G. Y. (55-5838), a 77-year-old woman, was first seen May 16, 1955. She was in excellent health until 3 years before admission. She had lost 33 pounds during the previous 2 years and had a chronic cough. Roentgenograms revealed massive atelectasis

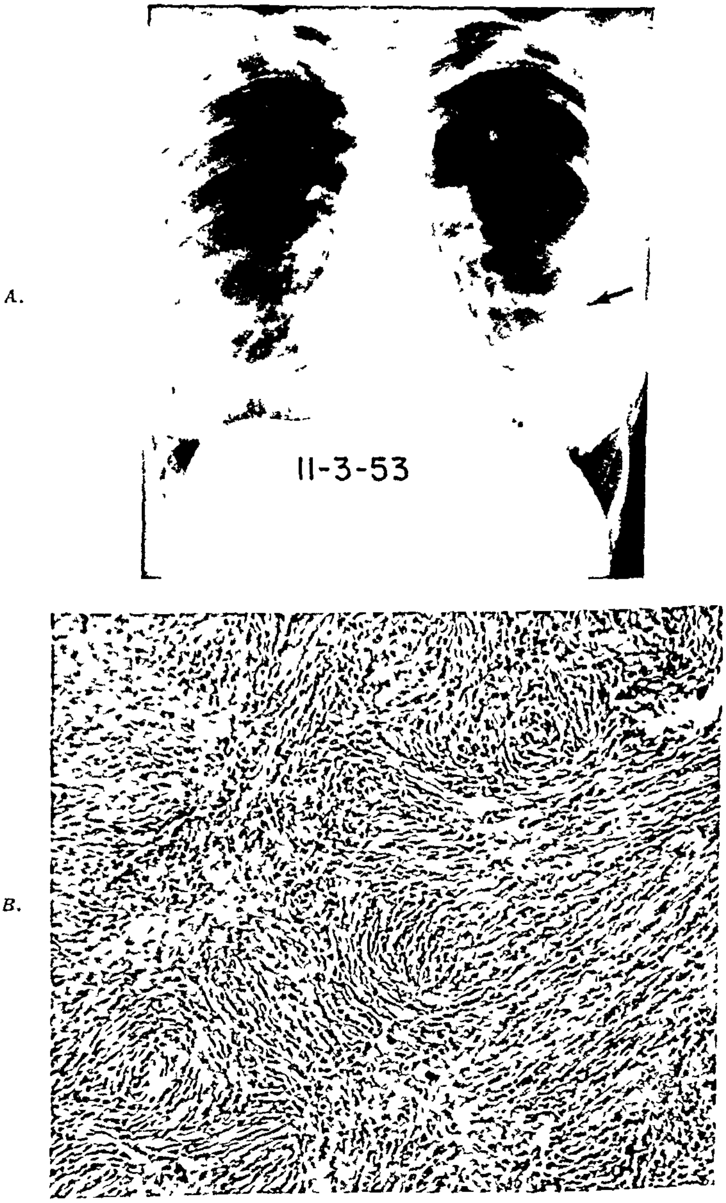


Fig. 2.—Case 3. *A*, Roentgenogram taken 2 years after resection of a benign mesothelioma on the left—recurrent lesion present in mid-lung field.
B, Microscopic section: Fibroblastic cells and interlacing connective tissue patterns are well seen.

of the left lung. Severe compression of the left main-stem bronchus was found on bronchoscopy. On May 20, 1955, a left pneumonectomy was done. A very large mass which compressed the upper and lower lobes was encountered. It was not attached to pulmonary tissue but seemed to arise over the mediastinal pleura. Removal of this mass was only possible by pneumonectomy. The pathologic report stated it was a slowly growing fibrosarcoma, well differentiated, probably arising in the interlobar fissure. The bronchi and several branches of the left pulmonary vein and artery were surrounded and compressed by tumor tissue. The postoperative course was uneventful. A letter from the home physician on July 3, 1959, stated that the patient had developed metastatic lesions in the subcutaneous areas over the left shoulder and back, biopsy of which revealed metastatic mesothelioma.

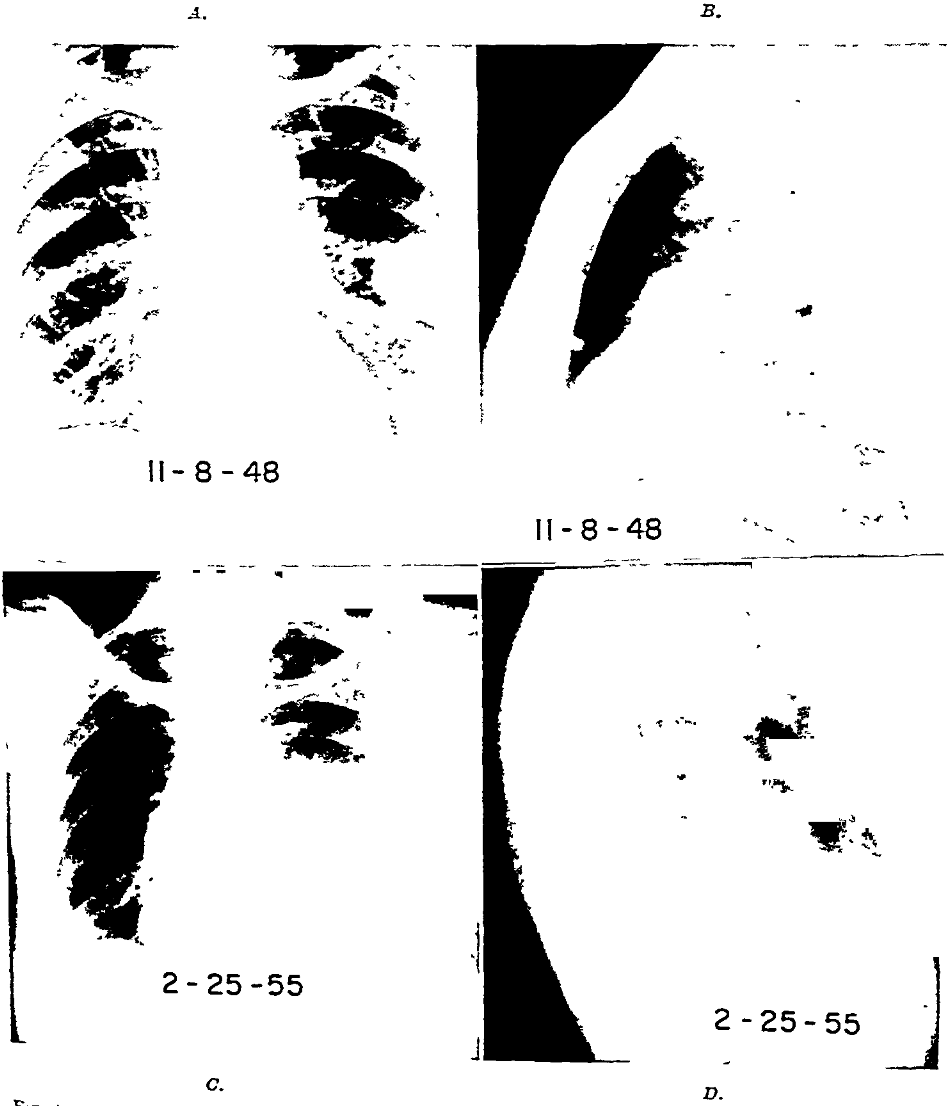


Fig. 2.—Case 5. A and B. Anterior and lateral roentgenograms demonstrating the lesion in November, 1948. C and D. Appearance of the same lesion during February, 1955.

CASE 8.—W. M. (57-10726), a 69-year-old man, was admitted to the Department of Urology on Aug. 22, 1957, with acute urinary retention due to benign prostatic hypertrophy. The patient also gave a history of having had some pedal edema and shortness of breath for 4 months. Routine roentgenograms revealed a large mass in the left posterior hemithorax in the supradiaphragmatic area. The clinical impression was that it was a neurogenic tumor or pleural tumor. A transurethral resection was done on Aug. 27, 1957. The postoperative course was uneventful. On Sept. 5, 1957, a left thoracotomy was carried out. A large mass was found in the left costophrenic sulcus and was resected. A pedicle, 2 by 3 cm. in diameter, was found attaching this mass to the basilar surface of the left lower lobe. The mass measured 16 by 13 by 7 cm. and weighed 900 grams. The pathologic report stated it was low grade pleural sarcoma-mesothelioma. The basic tumor forming cells were fibroblasts and fibrocysts which showed pleomorphism. The patient has been well since.

TABLE II. DIFFUSE MALIGNANT MESOTHELIOMA

CASE NO.	AGE AND SEX	DURATION OF SYMPTOMS	TIME LESION WAS KNOWN	DATE OF OPERATION	RESULT
9	64 M	5 mo.	?	None	Death 1 mo. after admission; widespread metastases
10	25 F	4 mo.	Pneumothorax, 4 mo.	8/19/48 Thoracotomy and biopsy	Death 4 mo. after diagnosis
11	37 F	1 mo.	?	2/20/53 Thoracotomy and biopsy	Death 4 yr. after diagnosis
12	68 F	2 mo.	2 mo.	3/10/55 Thoracotomy and biopsy	Death 9 mo. after diagnosis
13	59 F	1 mo.	1 mo.	10/19/55 Right pneumonectomy	Death 2 mo. after diagnosis
14	61 F	1 mo.	5 yr.	12/13/56 Thoracotomy and biopsy	Death 3 yr. after diagnosis
15	70 M	3 mo.	3 mo.	None	Death 2 weeks after admission
16	52 F	2 mo.	2 mo.	6/4/57 Thoracotomy and biopsy	Death 1 mo. after diagnosis

CASE 9.—D. D. (G 6971), a 64-year-old white male, was admitted on June 1, 1932. The entrance complaint was pain in the left side of the chest, weight loss, and dyspnea for 5 months. Roentgenograms revealed a massive left pleural effusion with displacement of the mediastinal structures to the right. The pleural fluid was aspirated and a pneumothorax was produced. The nodular appearance of the pleura suggested the presence of a pleural neoplasm. The patient died on Aug 14, 1932. Postmortem examination revealed the left pleural space to be filled with sero-fibrino-sanguineous fluid. The left lung was collapsed. The pleural surfaces were markedly thickened. The greatest part of the neoplasm was found over the diaphragmatic surfaces. Microscopic sections showed spindle-shaped cells. In areas, the neoplasm formed spaces which were lined by epithelial type cells. The neoplasm was invading lung, diaphragm, aorta, and had also metastasized to kidneys, liver, and the right lung. The final diagnosis was malignant mesothelioma.

Case 10.—G. W. (42-9041), a 25-year-old female secretary, experienced severe pain in her left shoulder and chest on April 14, 1948 (Figs. 4, *A*, *B*, and *C*). Roentgenograms showed a spontaneous pneumothorax and a small area of infiltration in the left upper lung field. The patient was admitted to the Oakdale Tuberculosis Sanatorium and there experienced four more left-sided spontaneous pneumothoraces. On Aug. 4, 1948, the patient developed severe generalized left chest pain and cough. There had been no fever, hemoptysis, or weight loss. Examination at that time revealed a left hydrothorax. The patient was admitted to the University Hospitals on Aug. 14, 1948. Thoracentesis produced 200 c.c. of thick serosanguineous fluid which, on examination, revealed no abnormal cells. Bronchoscopy and bronchograms were normal. On Aug. 19, 1948, a left thoracotomy was carried out. The pleura was found to be markedly thickened. On the posterior surface of the left upper lobe, a pedunculated mushrooming tumor of sarcomatous nature was encountered. It measured 8 cm. in diameter. This tumor was resected. There were many clots and large implants in the region of the costophrenic angle and over the diaphragmatic surface. A pathologic diagnosis of poorly differentiated, anaplastic neoplasm, probably mesothelioma, was made. The tissue was highly cellular and many mitotic figures were present. Large sheets of anaplastic oval and elongated cells of variable size with elongated hyperchromatic nuclei were seen. Conspicuous tissue spaces, varying from slit-like clefts to well-defined gland-like spaces, were lined by cuboidal mesothelial type cells. The patient's postoperative course was rapidly downhill. She developed signs of massive neoplastic infiltration of the left side of the chest which caused severe pain. The patient died on Dec. 7, 1948.

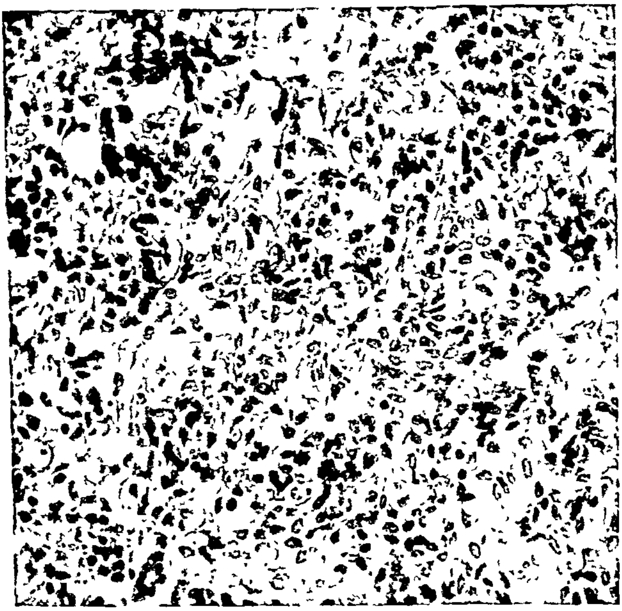
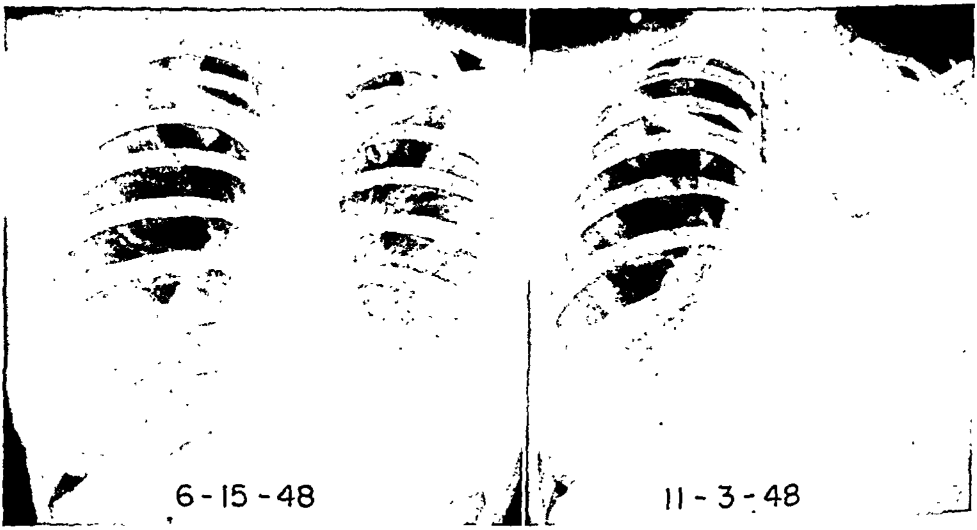


Fig. 3.—Cont'd. *E*, Microscopic appearance of the low grade fibrosarcoma

Case 11.—H. W. (53-1985), a 37-year-old white woman, was admitted from the Oakdale Tuberculosis Sanatorium on Feb. 16, 1953, with the complaint of increasing shortness of breath (Figs. 5, *A*, *B*, *C*, and *D*). Roentgenograms disclosed a massive right pleural effusion. Thoracentesis produced large amounts of serosanguineous fluid which, on examination, contained no malignant cells. On Feb. 20, 1953, a right thoracotomy was done. The pleural space was studded with numerous soft vascular neoplastic nodules. Most of the neoplasm was located over the diaphragm and over the lower portions of the pleural space. Excision of one of the larger masses was carried out. Pathologic sections revealed closely packed cells with oval and round nuclei. There was frequent mitosis. In many areas the cells were arranged perpendicularly to blood vessels. A pathologic diagnosis of pleural mesothelioma, diffuse type, was made. Postoperatively the patient was treated with irradiation therapy delivering 2,500 r through two portals. The patient was seen frequently and was completely asymptomatic until July of 1957 when she was admitted with the complaint of progressive weakness of 1 month's duration. The patient had some weight loss, and developed partial right third cranial nerve palsy, and diplopia. The diagnosis of severe



A. *B.*

Fig. 4.—Case 10. *A*, Roentgenogram which shows the small area of infiltration in left upper lobe. *B*, Roentgenogram taken 1 month before death of patient (left hemithorax overpenetrated). Note the large mass in left upper lung field and the neoplastic involvement of the left pleural space.

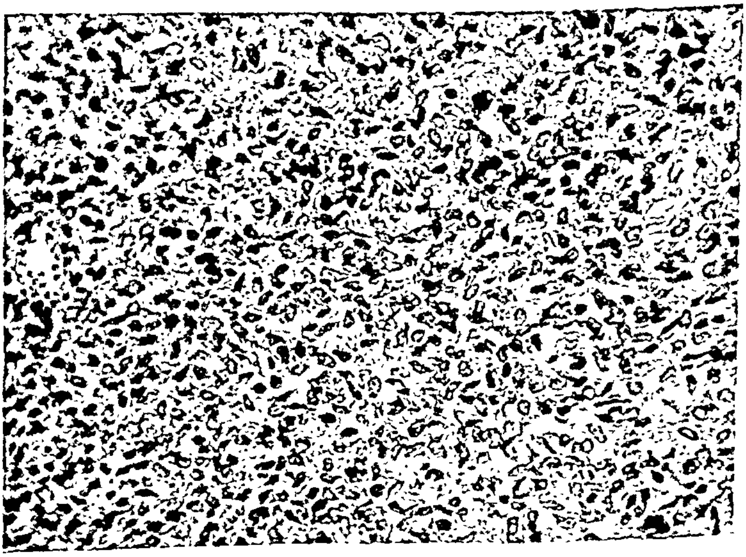


Fig. 4.—Cont'd. *C*, Microscopic section of biopsy: Highly cellular tissue with many mitotic figures. Note interspersed epithelioid cells.

myasthenia gravis was made. Mesitonin, 60 mg. 3 times daily, restored her normal strength. However, the patient's condition gradually deteriorated, necessitating tracheostomy. She died on Aug 5, 1957, in respiratory failure. Prior to the time of death there was some evidence of increase of the size of the right mediastinal mass. Postmortem examination was not obtained.

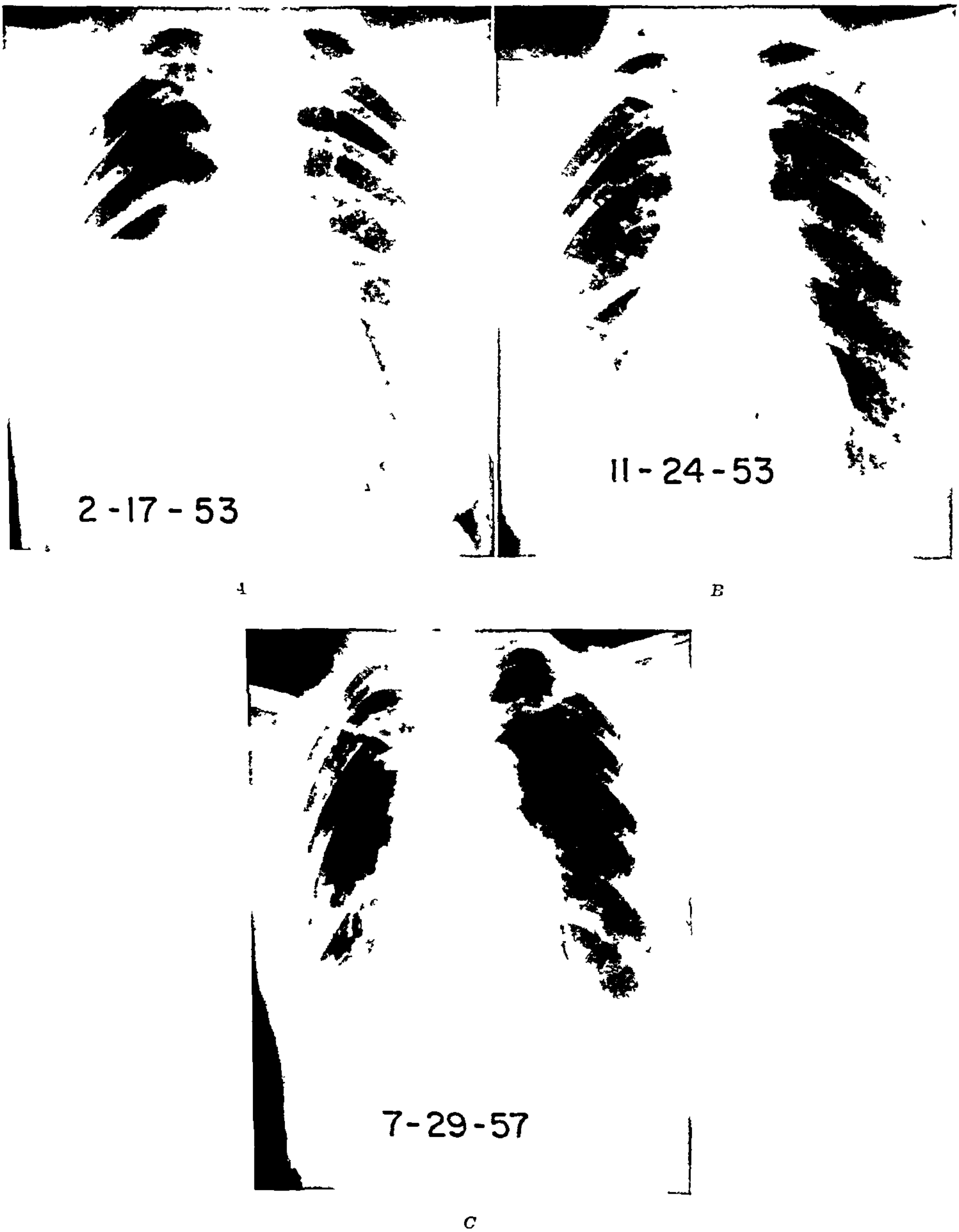


Fig 5.—Case 11. *A*, Roentgenogram which shows massive right pleural effusion with pneumothorax after thoracentesis in 1953.
B, Appearance of right lung after thoracotomy and irradiation therapy.
C, Roentgenogram taken 1 week before death of patient in 1957.

Case 12.—A. W. (55-2427), a 68-year-old woman, was admitted on Feb. 26, 1955, stating that she had had severe shortness of breath for about 2 months. She had had a right radical mastectomy 34 years before. On admission, a massive right hemothorax was encountered. Numerous thoracenteses were carried out. The pleural fluid failed to reveal abnormal cells. Bronchoscopy was normal. On March 10, 1955, an exploratory thoracotomy was carried out. A small neoplastic mass located over the posterior pleural parietal surface at the level of the ninth and tenth vertebral bodies was encountered. A large amount of serosanguineous fluid and blood clots were present in the pleural space, holding the lung in a collapsed state. *Frozen sections of the lesion gave the impression of fibrosarcoma* of the pleura. Decortication and re expansion of the lung were thought to be useless due to numerous neoplastic implants. Part of the primary lesion was excised. The pathologic report stated it was a cellular neoplasm with organizing inflammatory exudate, probably mesothelioma. The cells were spindle-shaped, closely packed with numerous mitotic figures.

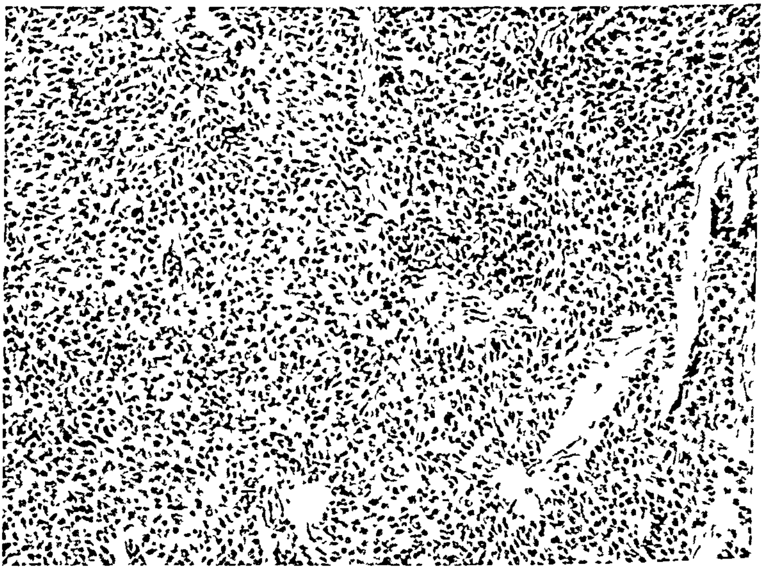
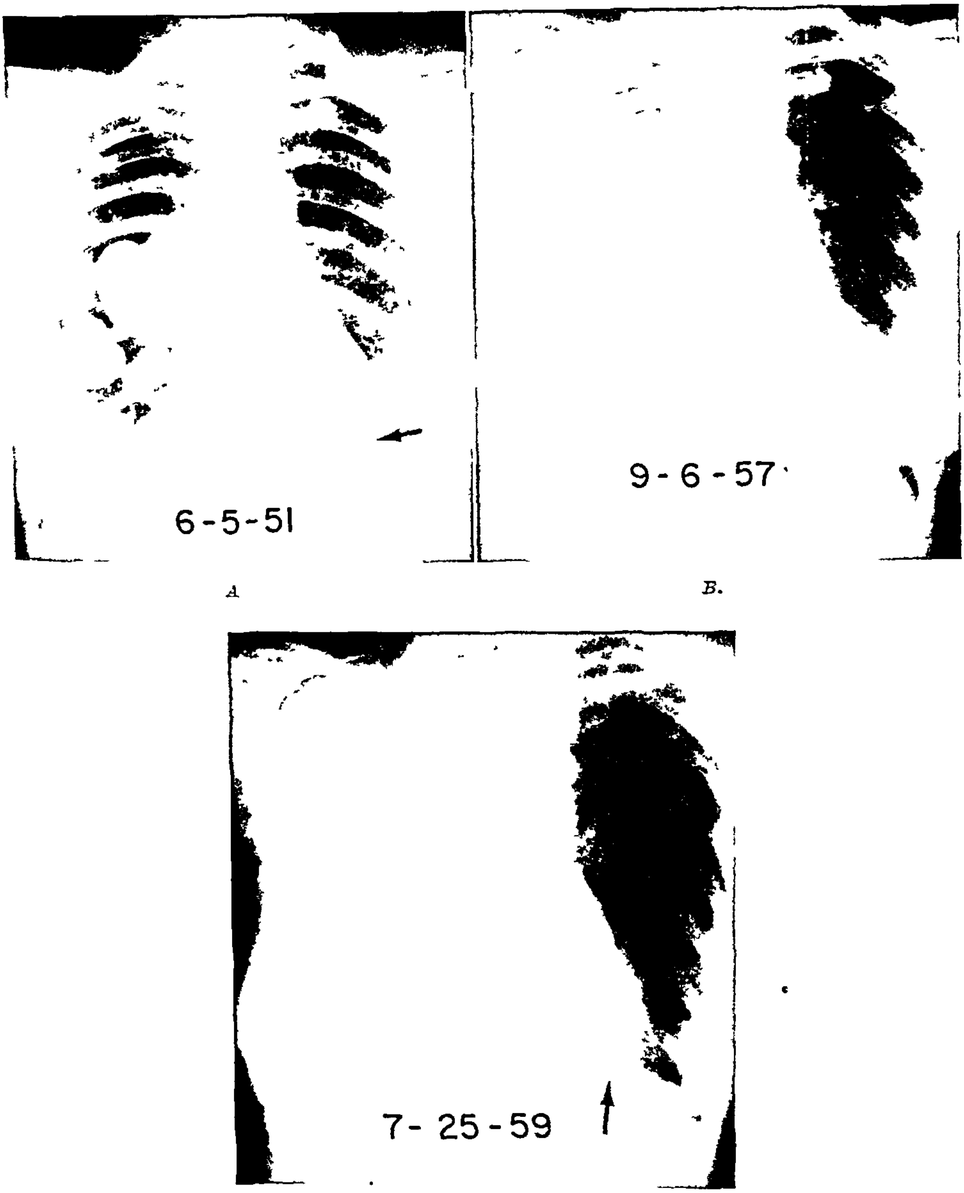


Fig 5.—Cont'd *D*, Microscopic appearance of tumor. Epithelial-like cells are seen.

In other areas the cells were arranged in tubular and papillary structures and had epithelial characteristics. The patient was discharged to receive irradiation therapy in her home town. The patient was readmitted on Dec. 18, 1955, complaining of severe right upper abdominal pain and some abdominal distention. A mass was palpable in the right upper quadrant of the abdomen. A barium enema showed the mass to be extrinsic to colon and displacing it to the left. At exploratory laparotomy performed on Dec. 21, 1955, ascites and generalized neoplastic spread over the peritoneal surfaces were found. The neoplasm was the same as the one seen during the previous operative procedure. The patient died on Jan. 24, 1956.

Case 13.—E. R. (55-12601), a 59-year-old woman, was admitted on Oct. 11, 1955, complaining of severe shortness of breath of 10 days' duration. She had been in apparently good health until 5 weeks before admission at which time she developed pain in the right side of her chest, a nonproductive cough, and temperature elevation up to 101° F. Roentgenograms revealed a mass in the right anterior hemithorax. Bronchoscopic examination was normal. Thoracentesis produced about 20 c.c. of bloody fluid which revealed no abnormal cells. On Oct. 19, 1955, a right thoracotomy was carried out. The pleura was invaded by neoplastic tissue. It was possible to free the neoplasm from the chest wall by extrapleural dissection. A right pneumonectomy was carried out encompassing all the visible neoplasm. The lung weighed 1,000 grams. A large tumor occupied the greater portion of the lung. It measured 12 by 14 by 6 cm. The tumor was soft, mucoid in consistency, and there was spread toward the root of the lung. Microscopic sections revealed malignant cells invading the lung in solid sheets The cells were pleomorphic



A

B.

C.

Fig 6—Case 14 A, Roentgenogram taken in 1951, 5 years before exploratory thoracotomy Note multiple well-circumscribed lesions on the right and less apparent lesions on the left

B, Massive pleural effusion present 9 months after exploratory thoracotomy.

C, Roentgenogram taken in 1959, 2 months before the death of patient. Note the absence of pleural effusion following irradiation and intrapleural Au^{198}.

CASE 12.—A. W. (55-2427), a 68-year-old woman, was admitted on Feb. 26, 1955, stating that she had had severe shortness of breath for about 2 months. She had had a right radical mastectomy 34 years before. On admission, a massive right hemothorax was encountered. Numerous thoracenteses were carried out. The pleural fluid failed to reveal abnormal cells. Bronchoscopy was normal. On March 10, 1955, an exploratory thoracotomy was carried out. A small neoplastic mass located over the posterior pleural parietal surface at the level of the ninth and tenth vertebral bodies was encountered. A large amount of serosanguineous fluid and blood clots were present in the pleural space, holding the lung in a collapsed state. Frozen sections of the lesion gave the impression of fibrosarcoma of the pleura. Decortication and re-expansion of the lung were thought to be useless due to numerous neoplastic implants. Part of the primary lesion was excised. The pathologic report stated it was a cellular neoplasm with organizing inflammatory exudate, probably mesothelioma. The cells were spindle-shaped, closely packed with numerous mitotic figures. In other areas the cells were arranged in tubular and papillary structures and had epithelial characteristics. The patient was discharged to receive irradiation therapy in her home town. *The patient was readmitted on Dec. 18, 1955, complaining of severe right upper* abdominal pain and some abdominal distention. A mass was palpable in the right upper quadrant of the abdomen. A barium enema showed the mass to be extrinsic to colon and displacing it to the left. At exploratory laparotomy performed on Dec. 21, 1955, ascites and generalized neoplastic spread over the peritoneal surfaces were found. The neoplasm was the same as the one seen during the previous operative procedure. The patient died on Jan. 24, 1956.

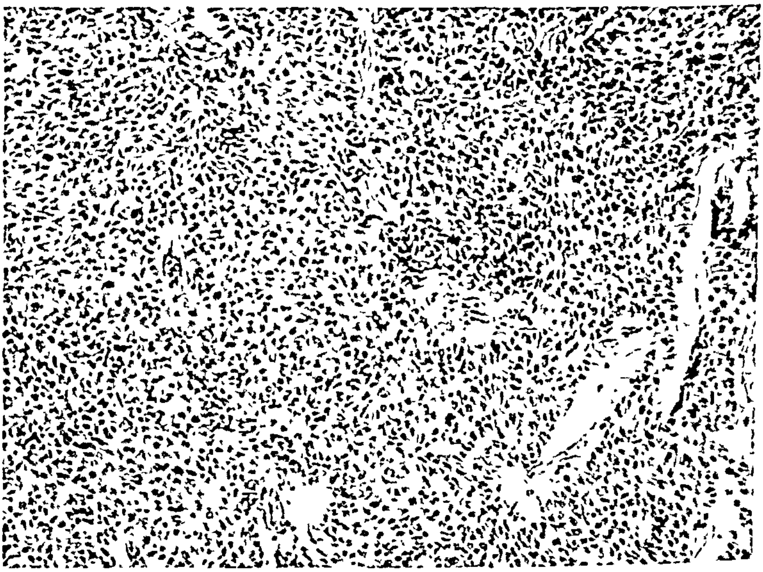


FIG. 5.—Cont'd *D*, Microscopic appearance of tumor. Epithelial-like cells are seen.

CASE 13.—E. R. (55-12601), a 59-year-old woman, was admitted on Oct. 11, 1955, complaining of severe shortness of breath of 10 days' duration. She had been in apparently good health until 5 weeks before admission at which time she developed pain in the right side of her chest, a nonproductive cough, and temperature elevation up to 101° F. Roentgenograms revealed a mass in the right anterior hemithorax. Bronchoscopic examination was normal. Thoracentesis produced about 20 c.c. of bloody fluid which revealed no abnormal cells. On Oct. 19, 1955, a right thoracotomy was carried out. The pleura was invaded by neoplastic tissue. It was possible to free the neoplasm from the chest wall by extrapleural dissection. A right pneumonectomy was carried out encompassing all the postmortem examination, an infiltrating tumor over the superior surface of the diaphragm, right lung, and extension into the right hilar lymph nodes was found. Microscopically it was shown to be an anaplastic neoplasm. The cells were spindle-shaped, very pleomorphic, with many mitotic figures. There were tumor cells along the lymphatic routes and, in areas, they had the appearance of an epithelial neoplasm. A final diagnosis of malignant mesothelioma was made.

CASE 16.—I. P. (57-7046), a 52-year-old woman, was admitted on May 27, 1957, with the complaint of shortness of breath for 2 months. Roentgenograms revealed a left pleural effusion. Several thoracenteses had been carried out before admission to the hospital. The local physician informed her that the fluid was gelatinous in nature. Cytologic studies of the fluid were negative. It was suspected that this patient might have a malignant pleural tumor. Edema of the mucosa of the left lower lobe bronchus was found on bronchoscopic examination. On June 4, 1957, a left thoracotomy was carried out. There was evidence of invasion of the intrathoracic fascia by malignant tissue. The neoplasm appeared to envelop the entire lung. There was a small amount of fluid between the lung surface and the parietal pleura. Biopsy of the lesion showed it to be an anaplastic neoplasm. The cells were suggestive of epithelial origin. A diagnosis of malignant mesothelioma was made. The patient was given irradiation therapy 2,000 r through anterior and posterior ports. The patient had gained some weight and strength when examined on Oct. 10, 1957. The left pleural effusion had lessened in amount. A letter from the local physician informed us that the patient died in July of 1958.

DISCUSSION

The age range in both groups of patients was 25 to 77 years. Women were more often affected by the malignant type of disease than men. Several interesting points, as far as symptoms are concerned, bear mentioning. Osteoarthropathy or clubbing which was often observed in other reported series[1, 3, 8] was not found in any of our patients. One woman (Case 5) stated she had some neuralgic pains in her arms but on examination nothing of note was found. Shortness of breath was a common complaint. It was due either to varying degrees of pleural effusions or to large intrathoracic masses encroaching upon the pulmonary air space. One patient (Case 3) stated on admission that she had recurrence of afternoon temperature elevations, the same symptom she had experienced before the first resection of a localized mesothelioma. She was found to have a small recurrent intralobar fibrous mesothelioma. Serosanguineous pleural effusions, recurrent and often massive, were present in all patients with diffuse malignant mesotheliomas. One patient (Case 5), with a localized fibrous mesothelioma known to be present for at least 7 years, was found to have a massive hemothorax. It has been pointed out by others that hemorrhagic effusions do occur in the localized type of this neoplasm and that this does not affect the operability or the favorable prognosis.[2, 8] One patient (Case 10), with a highly malignant and rapidly fatal tumor, had, as the initial symptoms, repeated pneumothoraces. The true nature of the illness was not recognized until the patient developed, in addition, a massive hemothorax. On exploration, the original, still localized, malignant lesion was found in the upper lobe. The lower pleural space was filled with extensive gravitational metastases. Similar cases have been reported by others.[4, 20] One of our patients (Case 14), who must be placed into the group of patients with diffuse malignant tumors, has been known to have multiple but, at first, localized bilateral lesions.[7] Roentgenograms demonstrated the and mitosis was prominent. The neoplastic cells blended with tissue which had the appearance of anaplastic epithelial cells. One hundred and twenty-five millicuries of Au^{198} was injected into the pneumonectomy space. The patient made an uneventful recovery and was discharged on Oct. 28, 1955. She was readmitted on Dec. 13, 1955, in extremis, and died on Dec. 16, 1955. Postmortem examination revealed pneumonitis in the remaining left lung. There was residual tumor in the pleura and periosteal tissues of the thoracic cage Microscopically it gave the impression of a sarcoma but in areas it simulated an anaplastic adenocarcinoma. Malignant pleural mesothelioma was the final diagnosis.

CASE 14.—D. H. (56-16262), a 61-year-old woman, was first seen at the University Hospitals in 1951 (Figs. 6, *A, B, C,* and *D*). Roentgenograms revealed several large tumors in the right and a smaller one in the left mid-lung field. The lesions were thought to be metastatic in nature. No primary site could be found. The patient was again seen in December, 1956, with the complaint of shortness of breath. The same large tumors were present in both lung fields. There also was a massive pleural effusion on the right. Thoracentesis produced 1,000 c.c. of grossly bloody fluid which did not contain malignant cells. On Dec. 13, 1956, a right exploratory thoracotomy and biopsy of the neoplasm was done. The tumors were pedunculated mesotheliomas. A pathologic diagnosis of the biopsy of mesothelioma of pleura, carcinomatous type, was made. The patient was given a course of irradiation therapy, 2,000 r to anterior and posterior lung fields, with little improvement The patient was readmitted on Sept. 10, 1957, with recurrent massive hemorrhagic effusion Seventy-five millicuries of Au^{198} was given intrapleurally. This resulted in reduction and final disappearance of the hemorrhagic effusion. She developed metastasis to the chest wall, the cranium, and left breast, all of which were treated by local irradiation therapy. The patient died during October of 1959.

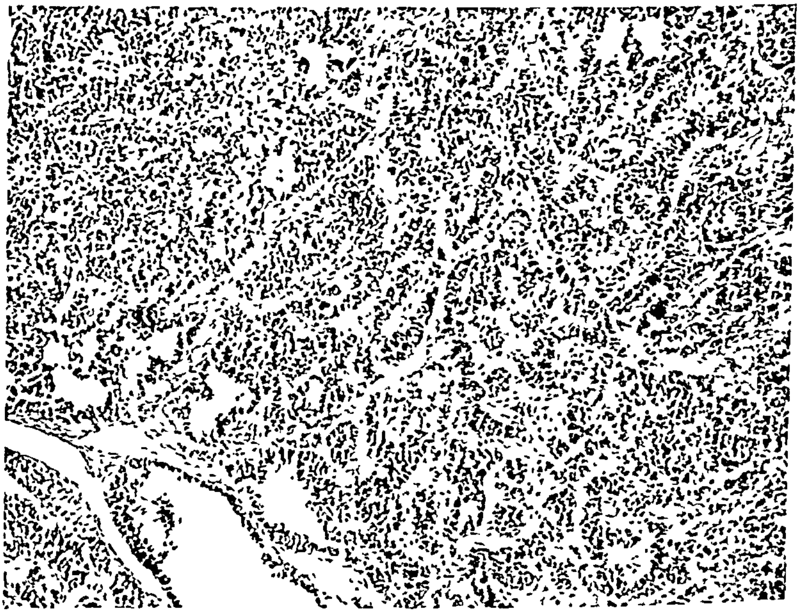


Fig 6—Cont'd *D,* Microscopic appearance of tumor. Note glandular and tubular arrangement of epithelial cells

CASE 15.—S. E. (56-707), a 70-year-old man, was admitted on Jan. 13, 1956, with the history of severe right-sided chest pain of 3 months' duration. Roentgenograms revealed opacification of the right hemithorax. There also was evidence of an intra-abdominal mass displacing gas-filled loops of bowel and stomach to the left. Thoracentesis on Jan. 16, 1956, produced 1,000 c.c. of serosanguineous fluid which was negative for malignant cells. Bronchoscopy revealed no endobronchial disease. The patient died on Jan. 29, 1956. At types is somewhat arbitrary and all gradations of these neoplasms are encountered. The presence of malignant epithelial cells in conjunction with malignant connective tissue elements, seen in the diffuse type of mesotheliomas, makes the prognosis very grave. The pleomorphism, frequent mitosis, and other histologic criteria associated with malignancy do not appear to affect the good prognosis for most patients after resection of well-encapsulated tumors. A correct diagnosis in this disease can only be made by exploration and biopsy of the nonresectable, or by removal of the localized, lesions.

ADDENDUM

Since submission of this manuscript, Patient A. B. (Case 6), who had a large localized pleural sarcoma resected on Mar. 28, 1955, was re-examined in February of 1960. Chest roentgenograms now show recurrence of a large pleural mass at the site of the original resection and multiple bilateral intrapulmonary metastases; however, the patient has no symptoms.

REFERENCES

1. Benoit, H. W., and Ackerman, L. V.: Solitary Pleural Mesotheliomas, J. THORACIC SURG. 25: 346-357, 1953.
2. Bogardus, G. M., Knudtson, K. P., and Mills, W. H.: Pleural Mesothelioma, Report of Four Cases, Am. Rev. Tuberc. 71: 280-290, 1955.
3. Clagett, O. T., McDonald, J. R., and Schmidt, H. W.: Localized Fibrous Mesothelioma of the Pleura, J. THORACIC SURG. 24: 213-230, 1952.
4. Eisenstadt, H. W.: Malignant Mesothelioma of the Pleura, Dis. Chest 30: 549 556, 1956.
5. Finby, H., and Steinberg, I.: Roentgen Aspects of Pleural Mesothelioma, Radiology 65: 169-182, 1955.
6. Godwin, M. C.: Diffuse Mesotheliomas: With Comment on Their Relation to Localized Fibrous Mesotheliomas, Cancer 10: 298 319, 1957.
7. Harris, M. S, Hyman, M. M., and Nevins, D. B.: Resectable Form of Multiple Mesothelioma, Dis. Chest 35: 127-133, 1959.
8. Heaney, J. P., Overton, R. C., and De Bakey, M. E.: Benign Localized Pleural Mesothelioma, J. THORACIC SURG. 34: 553-560, 1957.
9. Hochberg, L. A.: Endothelioma (Mesothelioma) of the Pleura, Am. Rev. Tuberc. 63: 150 175, 1951.
10. Kahn, D. S., Glay, A., and Madore, P.: Malignant Pleural Mesothelioma, J. THORACIC SURG. 38: 225 234, 1959.
11. Klemperer, P., and Rabin, C. B.. Primary Neoplasm of the Pleura, Arch. Path. 11: 385-412, 1931.
12. Maximow, A: Über das Mesothel (Deckzellen der serösen Häute) und die Zellen der serösen Exsudate. Untersuchungen an entzundetem Gewebe und an Gewebskulturen, Arch. fur exper. Zellforsch 4: 1-42, 1927.
13. McCaughey, W. T. E.: Primary Tumors of the Pleura, J. Path. & Bact. 76: 517-529, 1958.
14. Robertson, H. E.: Endothelioma of the Pleura, Am. J. Cancer Res. 8: 317-375, 1924.
15. Sano, M. E, Weiss, E., and Gault, E. S.: Pleural Mesothelioma—Further History of Its Histogenesis, J. THORACIC SURG. 19: 783-788, 1950.
16. Stout, A. P., and Murray, M. R.: Localized Pleural Mesothelioma—Investigation of its Characteristics and Histogenesis by the Method of Tissue Culture, Arch. Path. 34: 951-964, 1942.
17. Stout, A. P., and Himadi, G. M.: Solitary (Localized) Mesothelioma of the Pleura, Ann. Surg. 133: 50 64, 1951.
18. Tobiassen, G.: Mesotheliomas: Case Reports of Primary Pleural Tumours, as Well as One Presumably Primary Pericardial Tumour, and Suspicious Primary Pleural Tumours, Acta path. et. microbiol. scandinav. Suppl. 105, pp. 198-236, 1955.
19. Willis, R. A.: Pathology of Tumors, St. Louis, Mo., 1953, The C. V. Mosby Company.
20. Wolcott, M. W., Shaver, W. A., Walkup, H. E., and Peasley, E. D.: Mesotheliomas of the Pleura, Dis Chest 36: 119 126, 1959.
21. Yesner, R., and Hurwitz, A.: Localized Pleural Mesothelioma of the Epithelial Type, J. THORACIC SURG. 26: 325 329, 1953.

tumors 5 years before the patient was seen with a massive hemorrhagic effusion. The tissue biopsy proved the diagnosis of multiple malignant mesotheliomas of the carcinomatous type. This patient is one of 2 patients in this group who survived 3 years after the diagnosis had been made. The other patient (Case 11), with a diffuse malignant mesothelioma, survived 4 years. She died due to myasthenia gravis and respiratory failure. At the time of her death there was evidence of recurrent enlargement of the pleural and mediastinal masses. The other 6 patients with diffuse malignant mesotheliomas died within 9 months after the diagnosis had been established.

Six of the 8 patients in the group with localized fibrous mesotheliomas are alive and well, the most recent having been operated upon 2 years ago. One patient (Case 1) operated upon in 1927 died of a postoperative empyema. The other patient (Case 7) must be presumed to be dead. She was known to have extensive metastatic disease 4 years after pneumonectomy. Good palliation was obtained by this operation in the meantime. Localized fibrous mesotheliomas have a favorable prognosis but the microscopic picture may be one of great pleomorphism of cells and all degrees of malignancy. The tumors are usually well encapsulated and are easily removed for this reason. Only 1 patient (Case 2) in our series could definitely be classified as having a benign lesion. All the others showed definite evidence of pleomorphism of cells and malignant changes and these lesions were called pleural fibrosarcomas.

The appearance of the localized and diffuse tumors at operation is quite characteristic. There should be little difficulty in recognition and correct gross diagnosis. Frozen sections, however, at the time of exploratory thoracotomy, are usually misleading in the diffuse malignant group. The differentiation between this lesion and metastatic carcinomatous pleural involvement may be impossible. Surgical removal in the group of patients with localized fibrous tumors is the only hope for cure. Local resection of the lesion was possible in 5 of our patients. Two patients (Cases 2 and 4) required lower lobectomies with removal of the encapsulated adherent masses. One patient (Case 7) was subjected to pneumonectomy and this patient's tumor had infiltrated into the lung hilum.

In the group with diffuse malignant mesotheliomas, 2 patients were not operated upon. One patient (Case 13) had an extrapleural pneumonectomy but died 2 months thereafter due to rapidly advancing metastatic disease. Exploratory thoracotomy and diagnosis by biopsy were done in the remaining patients. Irradiation therapy which is said to have little benefit in this disease[5] was given to 4 of the patients (Cases 11, 12, 14, 16) with no benefit in 2 and good palliation in the others. Radioactive gold^{198} [2, 5] was used intrapleurally in 2 patients (Cases 13, 14). In 1 patient it was used in addition to external irradiation. It was of definite benefit in controlling the recurrent pleural effusions.

SUMMARY

Eight cases of localized fibrous and 8 cases of diffuse malignant mesotheliomas have been reported. The grouping of these neoplasms into two

On physical examination the child was dyspneic and obviously ill. The temperature was 98.6° F. The pulse rate was 106 per minute and respirations were 46 per minute. The blood pressure was 90/72 mm. Hg. The skin was pale and had a gray cast, without overt cyanosis. The tonsils were enlarged but not inflamed. The veins of the neck were slightly distended. The chest was symmetrical but there was a suggestion of increased anteroposterior diameter. Respiratory movements were short and panting. The lungs were clear to percussion and auscultation. Contrary to the findings before hospitalization, the heart was enlarged. The point of maximum impulse was at the fifth intercostal space in the anterior axillary line. A Grade 3 systolic murmur was heard at the left sternal border. The liver was tender and palpable five fingerbreadths below the costal margin. The peripheral pulses were strong. Slight pitting edema was present in the ankles and lower legs. No clubbing of the fingers or toes was noted.

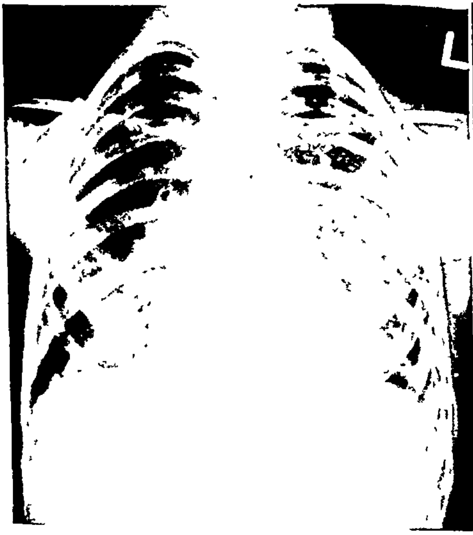


Fig. 1.

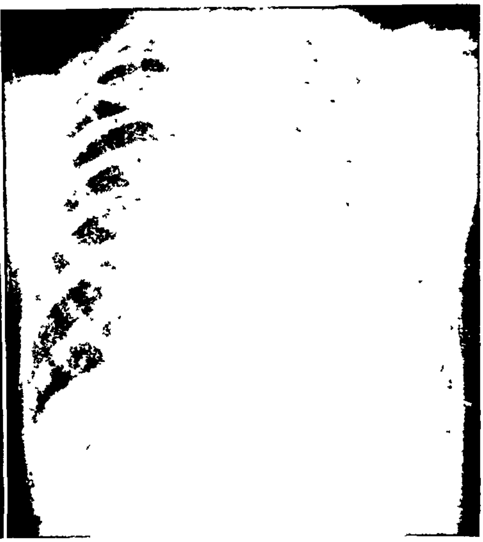


Fig. 2.

Fig. 1.—Roentgenogram of the chest at the onset of illness. The slight prominence of the right auricle and pulmonary artery was interpreted to be within normal limits.

Fig. 2.—Roentgenogram of the chest made 1 month later. Enlargement of the right auricle, ventricle, and pulmonary artery became evident Both main pulmonary arteries were prominent but peripheral vascular markings were diminished.

Results of examination of blood and urine were normal. The circulation time, using Decholin, was 18 seconds, arm-to-tongue. The venous pressure was 12.5 cm. saline. The tuberculin skin test was negative in the 1:1000 strength. The antistreptolysin titer was 100. Results of several blood cultures were negative.

Electrocardiograms revealed abnormal tracings characteristic of right ventricular hypertrophy or strain. Fluoroscopy and roentgenograms of the chest confirmed the cardiac enlargement, particularly of the right ventricle. Cardiac pulsations were diminished in amplitude. The pulmonary artery and its main branches were dilated but the vascular markings of the peripheral lung fields were diminished (Fig. 2).

Although the etiology was uncertain the clinical picture was one of severe right-sided cardiac decompensation. A diagnosis of congenital pulmonary stenosis with post-stenotic dilatation appeared most likely. Throughout the remainder of the clinical course, treatment consisted of oxygen inhalation, digitalization, diuretics, and restricted sodium intake. In spite of this treatment, the degree of cardiac failure progressed. The patient became more lethargic; tachycardia, hepatomegaly, and edema became more pronounced. The child died 7 weeks after the onset of illness and 3 weeks after admission to the hospital.

ISOLATED PULMONARY VENOUS SCLEROSIS: A CAUSE OF COR PULMONALE

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IT HAS BEEN KNOWN for almost two centuries that chronic pulmonary disease can produce untoward changes in cardiac function. The degree of such disturbances varies considerably and depends upon several factors which formerly were incompletely understood. In recent years investigations of cardiopulmonary disease have provided a wealth of dependable information with respect to the anatomic as well as the physiologic effects of pulmonary disease upon the heart.

Regardless of the cause, the effects upon the heart are so characteristic that the syndrome is described by a special term: pulmonary cardiac disease, or cor pulmonale. Of the many etiological agents discussed in the literature, which include primary pulmonary hypertension, emphysema and fibrosis, chronic inflammatory pulmonary disease and many others, there has not been a previous report of isolated pulmonary venous sclerosis as a cause of cor pulmonale.

Recent observations on a 5-year-old child who had fibrous obliteration limited to the pulmonary veins, which resulted in acute cor pulmonale, are pertinent to the problem of pulmonary cardiac disease.

CASE REPORT

A 5-year-old girl was a normal, active, and healthy child prior to her present illness. The prenatal history and birth were unremarkable. During infancy, routine physical examinations and immunizations against the common childhood diseases were provided. For 3 years prior to the present illness, no professional medical care had been necessary.

One month before being hospitalized the child had developed a skin rash and daily temperatures as high as 103° F. Ten days later, purulent material was noted in the canal of the right ear. A diagnosis of otitis media was made. By this time the rash had subsided somewhat but was still present. The rash was consistent with rubella but drug sensitization could not be excluded. The rash and the otitis media improved during the next 4 days with penicillin therapy. At this time bilateral basilar râles were first noted. The liver had become tender and was palpable three fingerbreadths below the right costal margin. The heart sounds were normal. Roentgenograms demonstrated clear lung fields and a cardiac silhouette that appeared to be within normal limits (Fig. 1). The results of examination of blood and urine were normal. Two weeks before admission to the hospital the child was dyspneic but did not have cyanosis or a cough. Because the shortness of breath became more severe, hospitalization became necessary.

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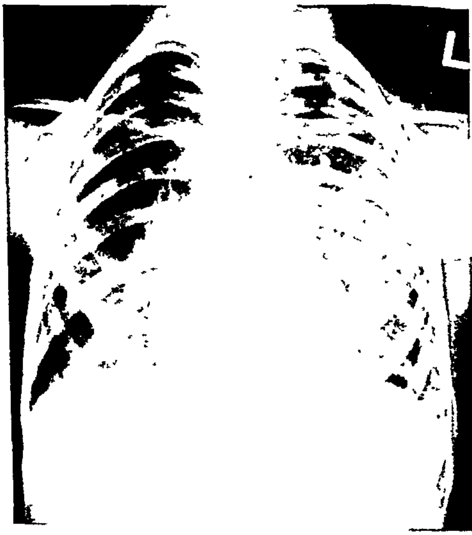

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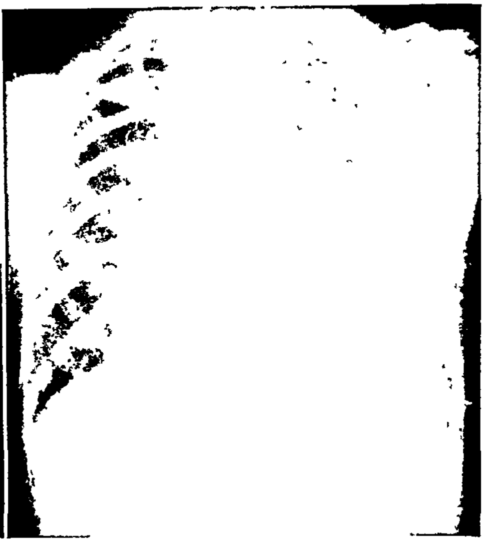

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Autopsy showed a normally developed and well-nourished female child. The skin was pale and had poor turgor but no cyanosis. Pitting edema was present in the lower legs. The abdominal cavity contained 200 c.c. of clear, straw-colored fluid. The liver was enlarged to a point 8 cm. below the right costal margin. Approximately 200 c.c. of clear fluid was present in each pleural cavity. The mediastinum was not remarkable except for the prominence of the venae cavae and the azygos vein. The bronchial arteries were small and entered the lungs from the aorta in a normal fashion.

The heart weighed 165 grams. The right atrium, right ventricle, pulmonary artery and its main branches were greatly dilated. The diameter of the pulmonary artery was twice that of the aorta. A friable mural thrombus, 1.5 cm. in diameter, was present in the right auricular appendage. The thickness of the right ventricular myocardium was 0.8 cm., equal to that of the left ventricle. Although the rings of the tricuspid and pulmonary valves were dilated, the valve leaflets were normal, as were the valvular rings and leaflets. The main pulmonary veins were slightly thickened but had adequate lumens. No congenital anomalies of the heart, or great vessels, or of the lungs could be identified.

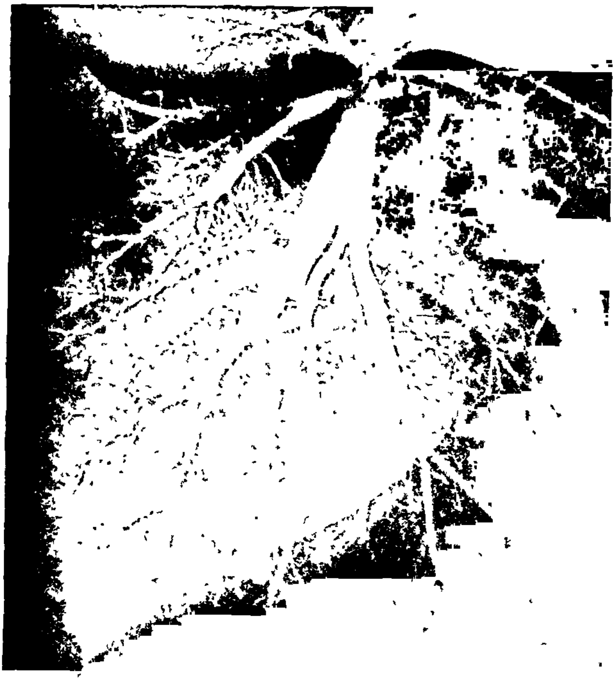

Fig. 3.—Postmortem arteriogram of the right middle and lower lobes. The contrast medium clearly outlines the pulmonary arterial tree, including the finer radicals No arterial occlusion is demonstrated

Microscopically, the mural thrombus in the right atrium was composed of a network of fibrin and formed blood elements. The thrombus showed no evidence of organization, thus indicating its relatively recent origin. Extreme hypertrophy of the myocardial fibers of the right atrium and ventricle was noted.

The right lung weighed 300 grams and the left one weighed 280 grams. Grossly, the lungs showed generalized poor aeration and congestion. Several small (0.5 cm. to 2 cm.) wedge-shaped, deep red infarcts were noted, located predominantly in the subpleural parenchyma. Postmortem roentgenographic contrast studies of the pulmonary arteries were normal, with the exception of the zones corresponding to small recent infarcts (Fig. 3).

Significant thickening of all pulmonary veins was the predominant feature of the pulmonary vasculature (Figs. 4, 5, 6, 8). The veins showed extensive fibrous proliferation involving the media and intima. There was partial to nearly complete obliteration of the small terminal venules and medium-sized veins. Larger veins were also involved but in a focal manner and to a lesser degree. The deposition of fibrous tissue in most of the pulmonary veins was dense and acellular (Figs. 6 and 8, *B*). Reticulum and collagenous fibers were concentrically arranged, completely choking off lumens or reducing them to narrow slits. No evidence of proliferation of elastic tissue was noted; all elastic fibers were confined to delicate adventitial structures.

Most of the cells associated with the fibrous tissues were small spindle-shaped fibrocytes. Occasionally, especially in areas where the collagen was less dense, fibroblasts were more prominent. Except for scattered histiocytes, inflammatory cells were not associated with involved pulmonary veins (Fig. 8). No vascular necrosis or acute phlebitis was found. The pulmonary arteries, in distinct contrast to the veins, were normal (Fig. 7). Identified by their close proximity to the bronchi and their characteristic mural structure, each artery presented a widely patent lumen, delicate intima, and discrete internal elastic membrane. A few small to medium-sized pulmonary arteries were completely occluded by recent unorganized emboli and were in the vicinity of small early pulmonary infarcts. The remainder of the lung showed congestion of alveolar capillaries, extravasation of blood and serum into air spaces, and focal atelectasis.

The liver weighed 760 grams. It was enlarged and had a tense capsule and a rounded lower edge. The parenchyma was finely mottled and was a deep reddish-brown. Microscopically, considerable centrolobular congestion was noted. Except for passive congestion, the remainder of the organs were grossly and microscopically normal. None of the organs of the body other than the lungs showed changes in the vessels.

The autopsy diagnosis was: Isolated pulmonary phlebosclerosis with (a) subacute cor pulmonale, (b) passive visceral congestion, and (c) mural thrombosis, right auricle, with pulmonary embolism.

DISCUSSION

Primary pulmonary vascular disease can be either congenital or acquired. In the former, multiple arteriovenous fistulas are of significance. Acquired pulmonary vascular disease is not a single etiological entity. Three processes give rise to sclerosis and obliteration of pulmonary arteries and arterioles. The first of these is pulmonary arteriosclerosis. Most of these cases are not true forms of arteriosclerosis but probably reflect secondary vascular changes incident to long-continued pulmonary hypertension.

Second, certain forms of vasculitis, especially acute necrotizing arteritis, periarteritis nodosa, and granulomatous arteritis may involve the lungs, either as a phase of the generalized disease or more rarely in an isolated form. It is probable that as time goes on many of the idiopathic sclerotic pulmonary vascular lesions will be classified as healed or burned-out varieties of "allergic" vasculitis.

Third, certain pulmonary vascular lesions are the result of repeated small emboli to the lung. Over a period of time such emboli lead to pulmonary arterial sclerosis through the process of thrombosis, organization, and attempted recanalization. In reality, these pulmonary vascular lesions should be excluded from the general group of primary vascular diseases since the source of embolism is usually outside the lungs, for example in the deep veins of the leg or in the heart.

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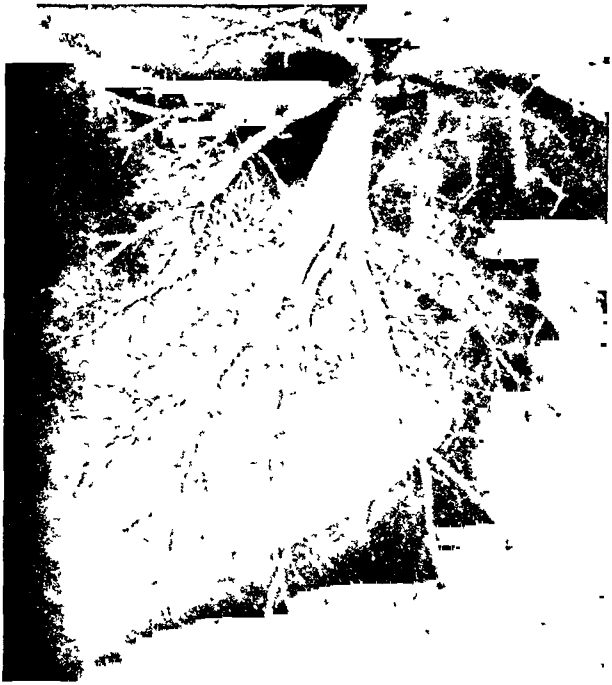

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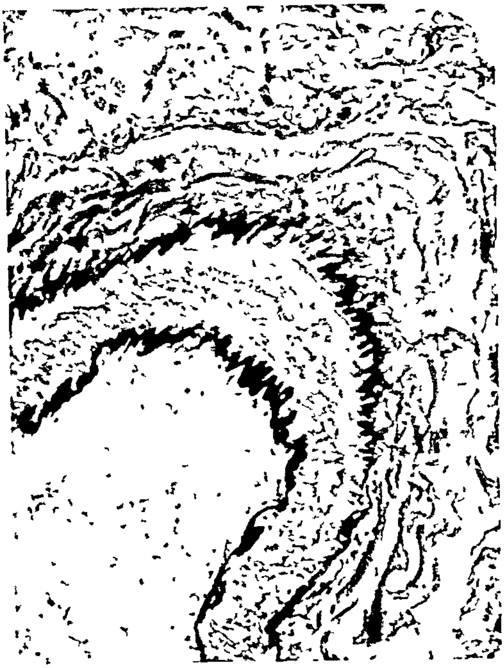


Fig 7—Medium-sized pulmonary artery in contrast to veins shown in Figs 5 and 6 Representative of all the pulmonary arteries with respect to normalcy, this vessel shows a widely patent lumen, delicate intima, discrete internal elastic membrane and a media of normal thickness (Weigert and van Gieson, ×200, reduced $\frac{2}{5}$)

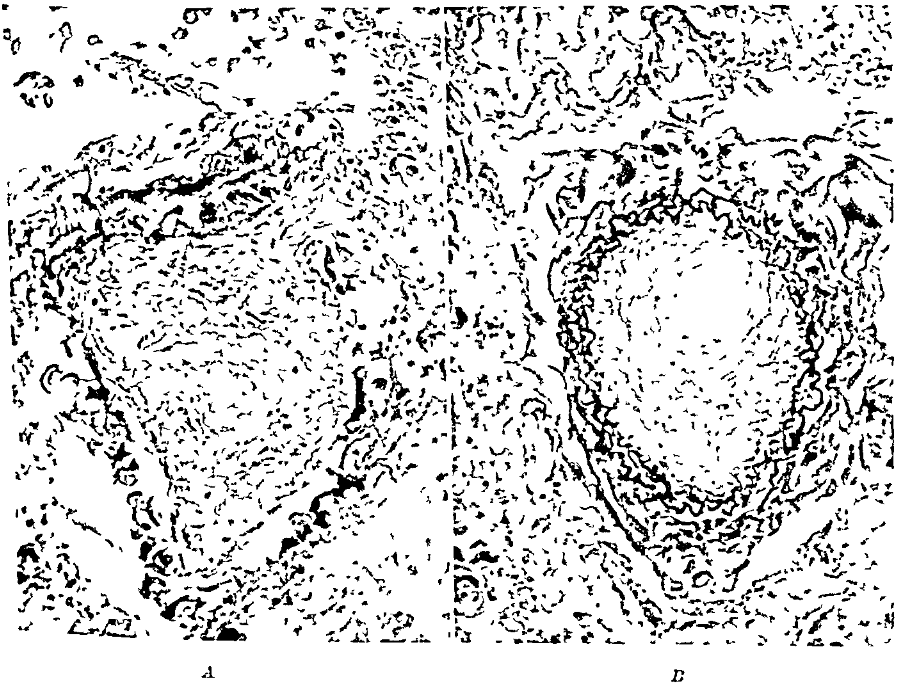
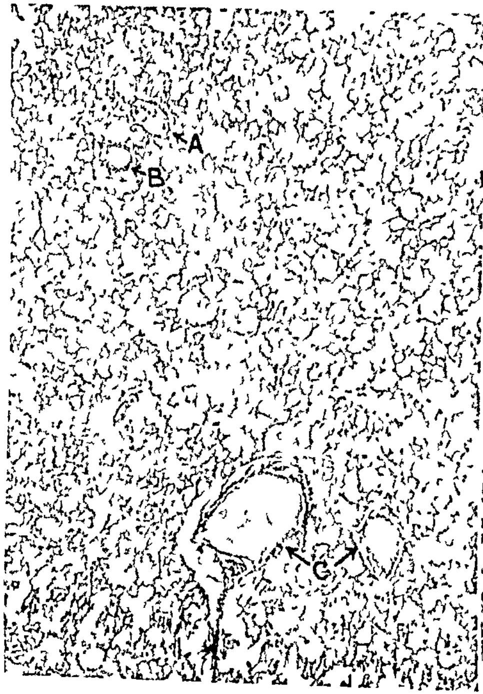


Fig. 8—*A* and *B*, Small pulmonary veins *A*, Complete obliteration of the lumens by concentrically arranged, dense collagenous fibrous tissue There is no evidence of organized thromboses or vasculitis. *B*, External elastic lamellae are delicate Note scattered histiocytes in the looser fibrous tissue of vein in *A* (Weigert and van Gieson, ×320, reduced $\frac{2}{5}$)



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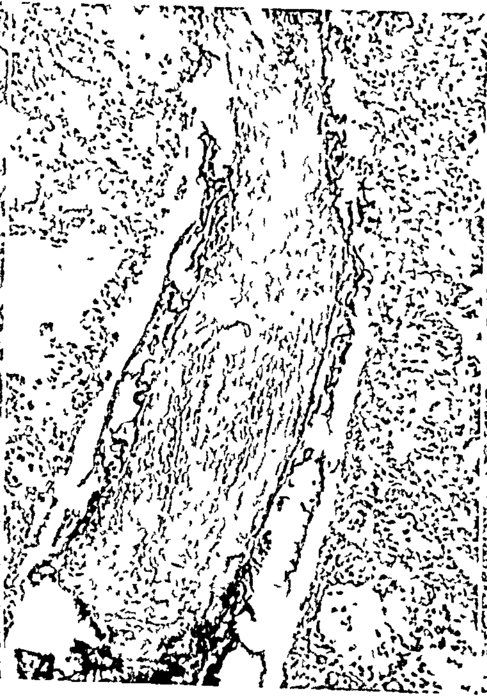


Fig 5

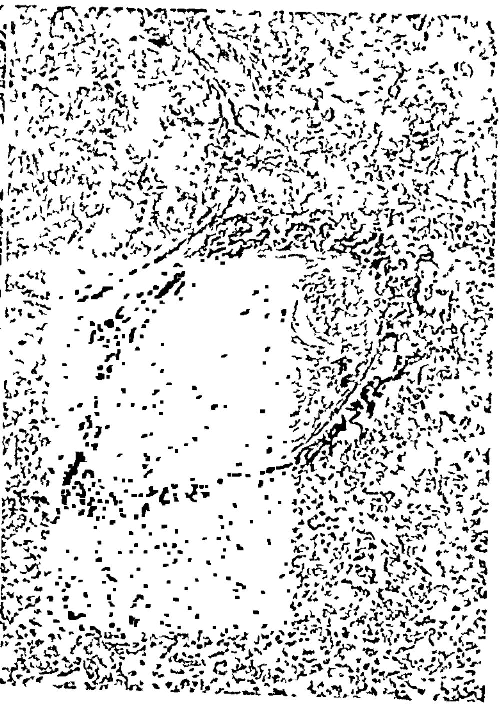


Fig 6

Fig. 4 —Representative area of pulmonary parenchyma demonstrating spatial relations between bronchi (*A*), pulmonary arteries (*B*), and pulmonary veins (*C*) The pulmonary arteries closely follow the course of the bronchi while the pulmonary veins course independently through lung parenchyma Venous occlusion is evident (Weigert and van Gieson stain, ×16; reduced ⅔)

Fig 5 —Medium-sized vein with its lumen reduced to minute caliber by massive fibrous thickening of the wall Adjacent parenchyma shows congestion (Weigert and van Gieson, ×100; reduced ⅔)

Fig 6 —Medium-sized pulmonary vein Dense collagenous fibrous tissue deposited throughout the media and subintima has reduced the lumen to narrow slits Almost all the medium-sized and small pulmonary veins showed this degree of change The adventitia appears relatively unaltered (Weigert and van Gieson ×200 reduced ⅔)

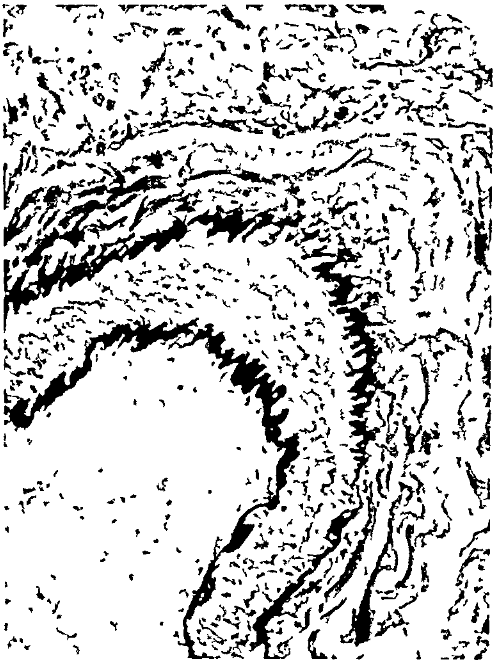
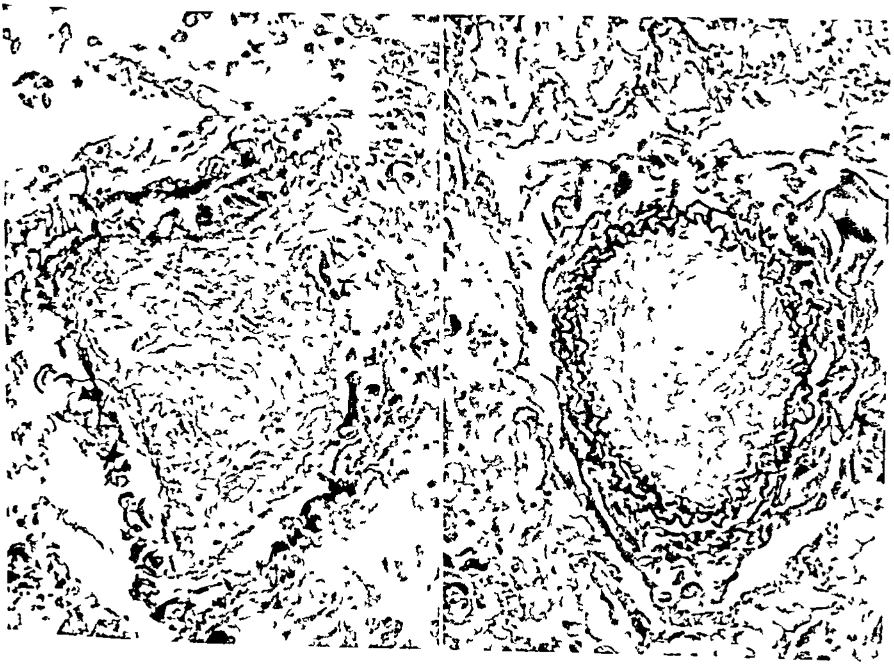


Fig 7 —Medium-sized pulmonary artery in contrast to veins shown in Figs 5 and 6 Representative of all the pulmonary arteries with respect to normalcy this vessel shows a widely patent lumen delicate intima discrete internal elastic membrane and a media of normal thickness (Weigert and van Gieson ×200 reduced ⅔)



A

B

Fig 8 —*A* and *B*, Small pulmonary veins *A*, Complete obliteration of the lumens by concentrically arranged, dense collagenous fibrous tissue There is no evidence of organized thromboses or vasculitis *B*, External elastic lamellae are delicate Note scattered histiocytes in the looser fibrous tissue of vein in *A* (Weigert and van Gieson, ×320, reduced ⅔)

Sclerosis of the pulmonary veins is occasionally noted in adults having primary pulmonary hypertension. The sclerosis, however, is always minimal and is overshadowed by the extensive involvement of the pulmonary arteries. Such focal areas of venous occlusion are probably secondary, reflecting stasis of the venous circulation, followed by thrombosis.

The literature was reviewed but no case was found similar to the one reported here. Pulmonary vascular disease in both adults and children involves primarily the pulmonary arteries and arterioles. Most of these conditions have been considered as inflammatory, or even "allergic" in type. Other lesions, especially those occurring in children, have been described as the result of medial hypertrophy and endothelial proliferation of arterioles, perhaps representing congenital malformations.

Little can be said concerning the etiology and pathogenesis of isolated pulmonary phlebosclerosis. Experimental and clinical studies have shown that arteriolization of venous systems leads to obliterative venous sclerosis. Nothing in this case suggested a generalized accession of arterial blood to the pulmonary veins.

In the case reported here there were features which suggest that the process was a result of panpulmonary phlebitis which produced obliterative sclerosis. There were no findings which would support an infectious or toxic etiological agent. Of some significance in this case was the early occurrence of a skin rash, thought at one time to be an allergic phenomenon.

SUMMARY

Obstructing sclerosis of the pulmonary veins has not been reported previously. In the case presented here, fatal cor pulmonale resulted from the unrelenting effects of obstruction of the pulmonary blood flow due to widespread venous sclerosis in the presence of a perfectly normal pulmonary arterial tree.

REFERENCES

1. Owen, W. R., Thomas, W. A., Castleman, B., and Bland, E. F.: Unrecognized Emboli to Lungs With Subsequent Cor Pulmonale, New England J. Med. 249: 919-926, 1953.
2. Parmley, L. F., Jr., and Jones, F. S.: Primary Pulmonary Arteriosclerosis, A. M. A. Arch. Int. Med. 90: 157-181, 1952.
3. Heard, B. E.: An Experimental Study of Thickening of the Pulmonary Arteries of Rabbits Produced by the Organization of Fibrin, J. Path. & Bact. 64: 13-19, 1952.
4. Eppinger, H., and Wagner, R.: Zur Pathologie der Lunge, Arch. f. inn. Med. 1: 83-146, 1920.
5. Brenner, O.: Pathology of the Vessels of the Pulmonary Circulation, IV., Arch. Int. Med. 56: 976-1014, 1935.
6. Cross, K. R., and Kobayashi, C. K.: Primary Pulmonary Vascular Sclerosis, Am. J. Clin. Path. 17: 155-162, 1947.
7. Wolman, M.: Hypertrophy of the Branches of the Pulmonary Artery, and its Possible Relationship With the So-Called Primary Pulmonary Arteriosclerosis in Two Infants With Hypertrophy of the Right Heart, Am. J. M. Sc. 220: 133-143, 1950.
8. Berthrong, M., and Cochran, T. H.: Pathologic Findings in Nine Children With "Primary" Pulmonary Hypertension, Am. J. Path. 30: 629-630, 1954.
9. Maxwell, I., and Wilson, R.: Cor Pulmonale in Infancy Simulating Congenital Heart Disease, Pediatrics 14: 587-600, 1954.

A NOTE ON THE TECHNIQUE OF MITRAL VALVULOTOMY

Allan E. Bloomberg, M.D., and Philip Glotzer, M.D., New York City, N. Y.

When the standard left anterolateral thoracotomy is used for mitral valvulotomy, difficulty is frequently encountered in fracturing the posterior commissure with the finger, whereas the anterior commissure is more readily fractured. It is difficult to bring the full power of the right index finger to bear on the posterior commissure with this approach.

Experience with the right-sided approach, described by Neptune and Bailey,[1] has demonstrated the ease of exerting more direct pressure to the posterior commissure. This technique, however, fails to accomplish obliteration of the left atrial appendage, which may continue to be a source for thrombus formation and embolization. In addition, difficulty has been encountered in reaching the valve through the Neptune and Bailey right-sided approach when the left atrium has been very large.

Ready access to both commissures and obliteration of the atrial appendage may be accomplished by positioning the surgeon to the patient's right, facing the patient, and utilizing a left anterolateral thoracotomy. The patient is placed in the right lateral semirecumbent position. A left inframammary incision is made and the pleural cavity is entered through the fourth interspace. The lung is retracted laterally and the pericardium is entered parallel to and either anterior or posterior to the phrenic nerve. After exploration of the external surface of the heart, a purse-string suture is placed at the base of the auricular appendage in such a fashion so that it may be incorporated in a Rumel tourniquet at the caudal end of the appendage. A Satinsky-type clamp is placed across the neck of the appendage distal to the purse-string suture. An incision is made on the lateral wall of the appendage. The operator's index finger (left or right) is inserted into the atrium as the Satinsky clamp is removed.

Following exploration of the atrium, the valve and its commissures, finger fracture of the commissures is performed. For fracture of the anterior commissure, the hand and finger are rotated slightly internally so that the flexor aspect of the tip of the finger engages the line of the anterior commissure at the valve orifice. Flexion of the finger in the line of the commissure permits the greatest application of direct force. With the orifice partially open, the chordae tendineae attached to the area of the posterior commissure may now

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be palpated. External rotation of the operator's right hand places the finger in a position to apply the same degree of direct force by flexion for fracture of the posterior commissure.

When initial palpation of the posterior commissure has revealed it to be short, it is advisable to open this commissure first, taking advantage of the fixation provided by the fused anterior commissure.

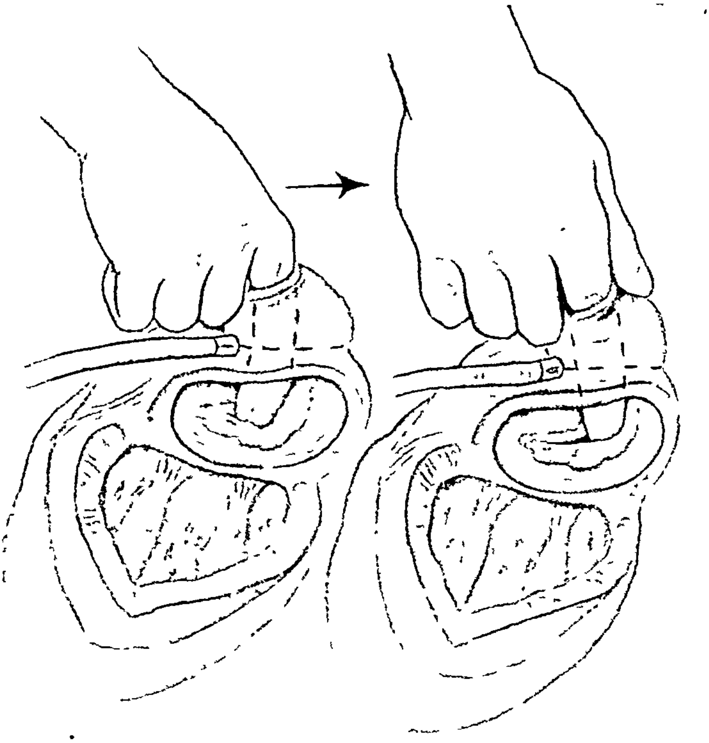

Fig 1—After the operator's finger is inserted into the atrial appendage, the anterior commissure may be felt by slightly rotating the hand and finger internally. External rotation of the hand brings the finger into position to palpate the posterior commissure The finger is in good position, against both commissures, to apply flexion action directly.

Closure is accomplished by ligating the base of the appendage and oversewing the atrial incision, after a portion of the appendage has been excised for histologic study. The use of supplemental commissurotomy knives has been virtually eliminated. However, cutting instruments may be inserted into the atrium with the same ease as from the left side.

Since adopting this approach, a complete commissurotomy has been performed with greater facility than with the classical left-sided approach.

REFERENCE

1. Neptune, W. B., and Bailey, C. P.: Mitral Commissurotomy Through the Right Thoracic Approach, J. THORACIC SURG. 28: 15, 1954.

Announcements

THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

Notice of Annual Meeting

The Forty-first Annual Meeting of The American Association for Thoracic Surgery will be held April 24, 25, and 26, 1961, in Philadelphia, Pennsylvania. Headquarters will be the Sheraton Hotel.

Requests for Hotel Reservations

These should be mailed directly to Mr. Brian Kirby, Reservation Manager, Sheraton Hotel, Philadelphia 3, Pennsylvania. Please mention this Association, the type of accommodation desired, the date, and approximate hour of arrival and departure. If accommodations are desired elsewhere please communicate directly with the hotel of your choice.

Material for the Program

SCIENTIFIC PAPERS.—Abstracts of all papers proposed for presentation at the 1961 meeting *must be received on or before* **November 15, 1960,** otherwise they will not be considered by the Program Committee. These should be labeled "For Thoracic Surgery Forum" or "For Regular Program" depending upon the nature of the subject matter, in the same manner as in previous years. They should contain from 200 to 250 words that accurately reflect the content of the completed paper.

Six, repeat, six clearly legible copies of *each* abstract must be sent to Miss Ada Hanvey, Administrative Assistant, The American Association for Thoracic Surgery, 308 Carondelet Building, 7730 Carondelet Avenue, St. Louis (Clayton) 5, Missouri.

Essayists selected for the program are reminded that papers presented at the meeting *must* be handed to the secretary *immediately* after their presentation. If they are not ready at that time there is a chance that they will not be published in THE JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY.

Applications for Membership

Applications for Associate Membership in the Association must be received by the Membership Committee *not later than* **November 15, 1960,** otherwise the application will be deferred for consideration until the 1962 meeting.

Applicants must be sponsored by three Active or Senior Members of the Association. In addition to the signature on the application form, the sponsors will forward a *separate* letter concerning the applicant directly to:

Frank Gerbode, M.D.
Chairman of the Membership Committee
Presbyterian Medical Center
San Francisco 15, California

Sponsors are reminded that *new* letters of recommendation must be forwarded to the Chairman of the Membership Committee should their applicants be held over for reconsideration a *second year.*

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Original Communications

STUDIES OF PERIPHERAL VASCULAR RESISTANCE ASSOCIATED WITH TOTAL CARDIOPULMONARY BYPASS

I. Peripheral Resistance Under Condition of Normothermia and Normotension

A. Robert Cordell, M.D. (by invitation), Merrill P. Spencer, M.D. (by invitation), and Jesse H. Meredith, M.D. (by invitation), Winston-Salem, N. C.

The availability of a satisfactory apparatus for conducting whole body perfusion has stimulated the development of a variety of techniques by different laboratories. Perfusion has been governed by attempting to control one or more physiologic modalities, including arterial flow rate, arterial blood pressure, venous oxygen tension, etc. However, it has been the common experience of numerous investigators that linear relationships between the modalities do not always occur. The failure of some of these linear relationships to remain parallel throughout total body perfusion has been credited in the past to changes in vasomotor tone. Alteration in vasomotor tone produces changes in total peripheral resistance which have been studied by several investigators.[1-5] Read and associates[5] studied the effects of alterations in vasomotor tone in both total peripheral resistance and pressure flow relationships in dogs undergoing total body perfusion by surgical ablation of the central nervous system or administration of vaso-active drugs. It was their opinion that total peripheral resistance in the intact state is made up of several components of

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From the Departments of Surgery and Physiology, Bowman Gray School of Medicine, Wake Forest College, Winston-Salem, N. C.

Aided in part by grants from the U. S. Public Health Service (H-3426, H-5257) and from the North Carolina Heart Association.

Read at the Fortieth Annual Meeting of The American Association for Thoracic Surgery at Miami Beach, Fla., May 11-13, 1960.

approximately equal magnitude, namely, nervous influences, inherent myogenic vascular tone, viscous properties of blood, and dimensional considerations in the completely relaxed vessels. McGoon and associates[3] studied 3 patients undergoing total body perfusion and found that mean arterial blood pressure became subnormal at the start of perfusion but returned progressively toward normal as the result of an increasing peripheral vascular resistance. These patients were perfused at normothermia utilizing a blood flow rate of approximately 2.3 L. per square meter of body surface per minute.

The purpose of the present study was to ascertain the change in peripheral vascular resistance associated with total body perfusion carried out under normothermic conditions and with the arterial flow rate adjusted to maintain a relatively normal arterial blood pressure.

METHODS

Eighteen dogs whose weights ranged from 11.0 to 16.5 kilograms (average 13.0 Kg.) were lightly anesthetized with thiopental sodium. Polyethylene cannulas were then inserted into the left femoral artery and vein. These cannulas were connected to Statham strain gauges for pressure recordings. The carotid artery was isolated in the neck for eventual insertion of the inflow cannula. A right thoracotomy through the fifth intercostal space was performed, after which the pulmonary artery was dissected from the aorta and the cardiac output measured. This measurement, using the Bowman Gray square wave electromagnetic flowmeter, has been previously described[6] and consists of the placement of a noncannulating flow probe around the ascending aorta to allow the measurement of ascending aortic flow. Studies were then begun by recording cardiac output (with the exception of coronary flow), arterial pressure, venous pressure, electroencephalogram, and electrocardiogram on a multichannel recorder.

The arterial inflow line from the rotating disc oxygenator was inserted into the carotid artery, after which a single ⅝ inch outflow cannula was placed through the right atrial wall extending into the right ventricular cavity. Total cardiopulmonary bypass was begun with the pulmonary artery completely occluded either by tape or clamp. Similar monitoring of the abovementioned modalities was carried out during the entire period of bypass with the exception that, during bypass, flow was measured on the arterial line of the bypass unit using the same electromagnetic flowmeter.[7, 8] During perfusion arterial pressure was maintained within 20 mm. of values before bypass by adjusting pump speed. Temperature was controlled within 2.5° C. by means of the Brown-Emmons heat exchanger inserted in the arterial line. Following a 30-minute perfusion, attempts were made to equilibrate pre-prefusion blood volume in the animal with blood from the oxygenator. Monitoring was continued and repeat aortic flows were measured in the ascending aorta for periods of 30 minutes to 1 hour after bypass. At intervals throughout the procedure, blood samples were drawn for oxygen content, pH, and hematocrit. All animals were sacrificed following the completion of the experiments.

Approximately 50 points were selected at appropriate intervals on the monitor record, pressures and flows were calculated, and total peripheral resistance calculated from the formula:

$$\frac{\text{Mean arterial pressure (mm. Hg)} - \text{Mean venous pressure (mm. Hg)}}{\text{Blood flow (ml./min.)}}.$$

The results of these studies have been plotted in graph form to depict changes which occurred.

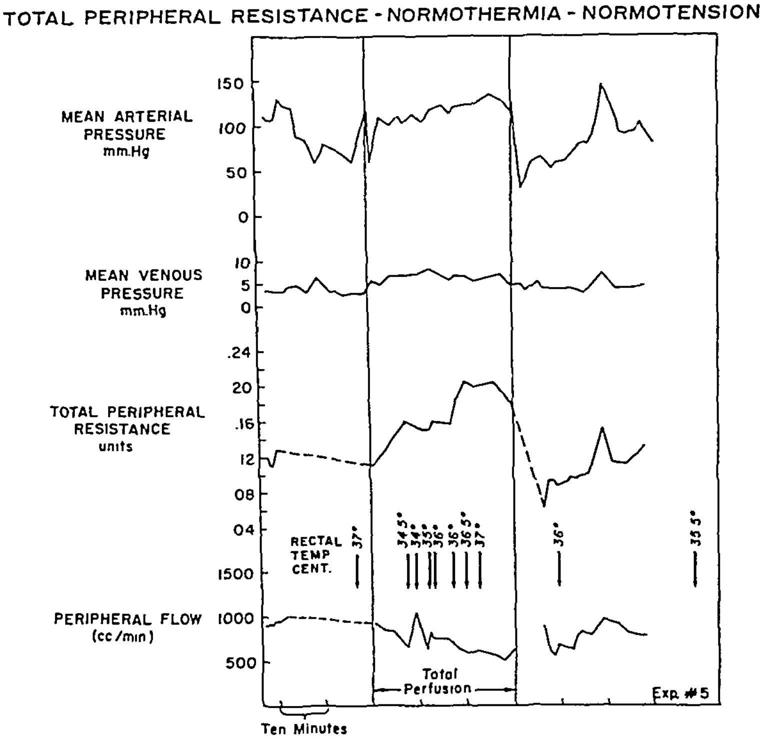

Fig. 1.—This graph was formed from points selected at regular intervals from the monitor record. Note the rise in resistance during bypass and immediate fall afterward.

RESULTS

Eight studies were discarded because of technical reasons which made the experiment inadequate. The reasons usually centered around sequestration of blood in the portal vascular bed and/or abnormally high rises in venous pressure. Fig. 1 depicts a typical experimental record showing arterial and venous pressures, flow rates before, during, and after bypass, and calculated vascular peripheral resistances. Of note in this record, as well as in others, is the drop in arterial blood pressure just prior to institution of total bypass due to interference with venous return at the insertion of venous catheters.

It can be seen that the average cardiac output in these animals falls somewhat below established norms as measured in our laboratory as well as by others. A comparison of the average cardiac output, as measured by the flowmeter with the output of the pump during bypass, can be seen in Fig. 2 which demonstrates in general the diminution in flow as governed by the conditions of these experiments.

Average peripheral vascular resistance units have been calculated for the period prior to bypass, the first 15 minutes of bypass, and the second 15

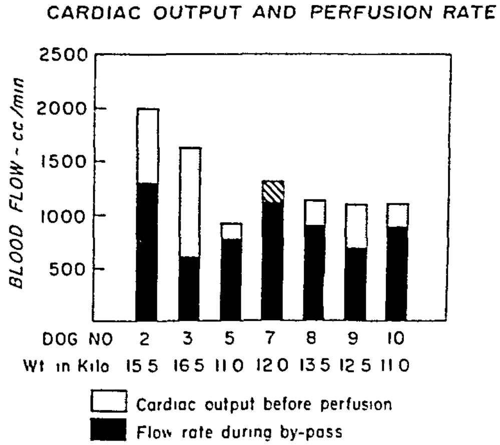

Fig. 2.—These experiments demonstrate the decrease in flow rate during perfusion as compared with cardiac output before bypass. Dog 7 is the lone exception where perfusion rate actually exceeded cardiac output slightly.

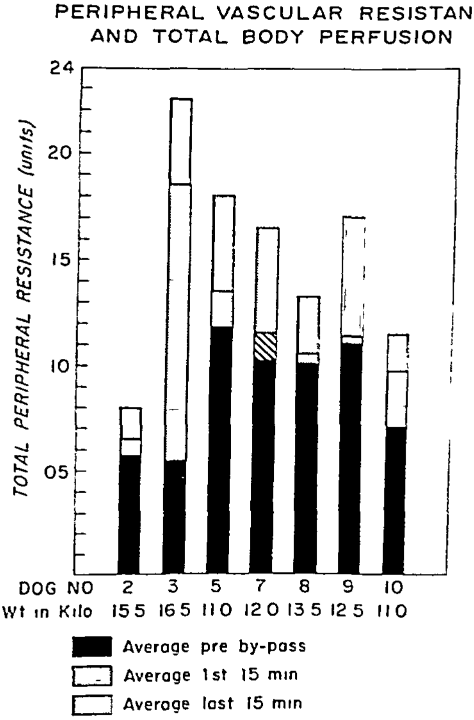

Fig. 3.—These experiments show the characteristic increase in resistance during the period of bypass. Dog 7 developed increased resistance initially but showed a fall below pre-bypass levels toward the end of perfusion.

minutes of bypass, and are shown on Fig. 3. These typical experiments show a uniform increase in peripheral vascular resistance which becomes more marked toward the latter period of the bypass, except for experiment 7 which showed a slight fall in peripheral resistance after an initial rise. The reason for this finding has not been explained on the basis of conditions of the experiment in that this animal was subjected to the same standard conditions as all others.

Total oxygen consumption has been averaged from the determinations made both before and during bypass to allow a comparison of these figures as shown in Fig. 4. Under the conditions of these experiments it can be seen that there was a significant decrease in oxygen utilization during bypass as compared with the period before bypass.

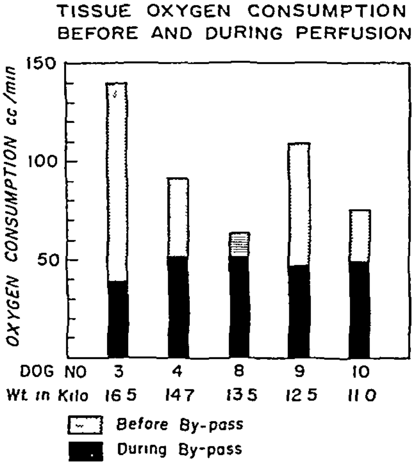

Fig. 4.—Oxygen consumption (calculated from arteriovenous difference and flow rate) consistently fell in all experiments during perfusion as shown in this graph. In some instances (Nos 3 and 9), this reduction amounted to more than 50 per cent.

pH values were consistently in the alkalotic range before bypass and, in general, came back toward normal levels during the bypass. The lowest pH recorded during bypass in any of these experiments was 7.32 and this level was maintained for only 5 minutes prior to a rise toward normal levels. pH values generally dropped toward the acidotic range in the period immediately after bypass and in a few experiments were in the range of 7.29 within 30 minutes after bypass. Carbon dioxide content was not measured frequently enough to allow adequate study of buffer base values.

COMMENTS

It is of interest that the average cardiac output from these animals as measured before bypass is below levels considered to be normal as measured by the Fick principle and by inlying flowmeter probes in awake animals. Presumably, diminution in cardiac output is produced to some extent by anesthesia and, in part, by thoracotomy and dissection around the great vessels. It was considered in these experiments that blood loss per se was not a major factor, in view of the fact that great care was taken to assure adequate hemostasis with minimal blood loss during the procedure. On the other hand, flow required to maintain normotension within the given limits during bypass generally fell far below the cardiac output before bypass. According to our current concepts of bypass management, these animals certainly underwent low flows during these experiments. Further evidence of low flow is mirrored by the diminution of oxygen consumption, as well as a tendency toward increasing A-V difference during the bypass.

Elevated pH figures before bypass were almost certainly due to hyperventilation with removal of carbon dioxide and development of a respiratory alkalosis. Since 100 per cent oxygen was used in the oxygenator, we can assume that the maintenance of normal pH during the period of bypass was in a large part due to hypocapnea. This "false" pH maintenance and its ability to mask a progressive metabolic acidosis has been emphasized by Moore.[9]

The rise in peripheral vascular resistance in this study is possibly related to the above-mentioned low flows with attendant development of oxygen debt during perfusion. It is well known that prolonged hypoxia eventually leads to vasodilatation with a pronounced drop in peripheral resistance as seen in severe hemorrhagic and/or traumatic shock. However, in view of the fact that these perfusions were of relatively short duration, it might be that the initial change is one of an increase in peripheral resistance which could be seen to fall if conditions of perfusion were allowed to prevail for a longer period.

It is of interest that this elevated total resistance dropped promptly upon returning the circulation to the animal's heart and lungs. Ankeney[1] has found this same phenomenon in dogs when they were perfused with low flow rates (50 c.c./Kg./min.). He believes that it reflects pooling in inaccessible vascular beds.

Another possible explanation for the increasing peripheral vascular resistance during total body perfusion is that afferent vagal endings situated in the right atrium cause a generalized vagal type constriction as a result of the fall in venous pressure in the atrium brought by the nature of venous cannulation itself. This reflex is thought to be responsible in part for the vasoconstriction which occurs as the usual response to hemorrhage and surgical shock.[10] Both of these conditions are associated with fall in venous pressure.

The well-known tendency of the dog to sequestrate blood in the portal system was seen in some of these experiments. All studies were discarded when significant blood loss from the oxygenator, or hepatic engorgement, or abnormal rise in inferior vena caval pressure was demonstrated. Nevertheless, minor degrees of sequestration could occur and conceivably could contribute to changes in peripheral resistance as seen here.

CONCLUSIONS

1. The governing of total cardiopulmonary bypass solely by maintenance of pre-bypass arterial pressure is by no means a safe criterion of adequate total body perfusion.

2. Under conditions of normothermia and normotension during total cardiopulmonary bypass in the dog, total peripheral vascular resistance tends to increase during a 30-minute bypass period and to drop sharply immediately upon returning circulation to normal.

3. Under these conditions arterial blood flow corresponding to cardiac output is materially reduced over basal cardiac output before bypass.

4. A marked decrease in oxygen uptake by the tissues during the bypass reflects this diminution in arterial flow.

5. Apparently adequate pH range can be maintained under the conditions of these experiments for periods of 30 minutes, but this pH range might well be maintained "falsely" by diminution in carbon dioxide partial pressure.

REFERENCES

1. Ankeney, J. L.: Personal communication.
2. Moffitt, E. A., Patrick, R. T., Swann, H. J. C., and Donald, D. E.: A Study of Blood Flow, Venous Blood Oxygen Saturation, Blood Pressure and Peripheral Resistance During Total Body Perfusion, Anesthesiology 20: 18-26, 1959.
3. McGoon, D. C., Moffitt, E. A., Theye, R. A., and Kirklin, J. W.: Physiologic Studies During High Flow, Normothermia, Whole Body Perfusion, J. THORACIC SURG. 39: 275-287, 1960.
4. Read, R. C., Johnson, J. A., and Kuida, H.: Systemic and Coronary Pressure Flow Relationships During Total Body Perfusion in the Dog, Am. J. Physiol. 190: 49-53, 1957.
5. Read, R. C., Kuida, H., and Johnson, J. A.: Effects of Alterations in Vasomotor Tone on Pressure Flow Relationship on the Totally Perfused Dog, Circulation Res. 5: 676-682, 1957.
6. Spencer, M. P., Cordell, A. R., Denison, A. B., Jr., Barefoot, C. A., and Spencer, H. H.: Measurement of Blood Flow in Experimental Animals by Means of Implanted Electromagnetic Probes, Fed. Proc. 18: 150, 1959.
7. Cordell, A. R., and Spencer, M. P.: Electromagnetic Blood Flow Measurement in Extracorporeal Circuits: Its Application to Cardiopulmonary Bypass, Ann. Surg. 151: 71-74, 1960.
8. Spencer, M. P., Cordell, A. R., Denison, A. B., Jr., and Barefoot, C. A.: A Direct Reading Flowmeter for Extracorporeal Circuits. Proc. Southern Soc. for Clinical Research, vol. 64, 1959; Am. J. Med. 27: 326, 1959.
9. Moore, F. D.: Metabolic Care of the Surgical Patient, Philadelphia, 1959, W. B. Saunders Company.
10. Best, C. H., and Taylor, N. B.: Physiological Basis of Medical Practice, Baltimore, Williams & Wilkins Co.
11. Green, H. D., Lewis, R. N., Nickerson, N. D., and Heller, A. L.: Blood Flow, Peripheral Resistance, and Vascular Tonus With Observations on the Relationships Between Blood Flow and Cutaneous Temperature, Am. J. Physiol. 141: 518-536, 1944.
12. Wiggers, H. C.: Cardiac Output and Total Peripheral Resistance Measurements in Experimental Dogs, Am. J. Physiol. 140: 519-534, 1944.

DISCUSSION

DR. C. FREDERICK KITTLE, Kansas City, Kans.—Dr. Adams, the previous paper and the discussers have placed particular stress on the arterial side of the vascular unit that is being perfused. I should like to call attention to the fact that this is not a singular vascular unit, but is, actually, a series of units, each with various factors controlling not only the arterioles but also the capillaries and veins.

We have approached the problem of attempting to segregate these by delineating the factors responsible for the return of blood from the inferior and the superior venae cavae.

One can determine the relative per cent of venous return through these two main parts of the body. Then by altering the flow rate of the pump, by the administration of drugs, by lowering the body temperature, or by producing hypoxia, one can determine various regional factors controlling resistance.

Very briefly, we have found that, although the perfusion rate remains constant, so that the total venous return is constant, the administration of neosynephrine, for instance, results in a relative and absolute increase of flow through the superior vena cava. Arfonad and hypoxia have a similar action.

I am calling attention to this because various regional manifestations may be important with long-term perfusion, or with perfusion at lower temperatures, more so than is presently recognized.

DR. DWIGHT C. MC GOON, Rochester, Minn.—This excellent paper by Dr. Cordell, as well as the final paper by Dr. Sanger, in addition to the many remarks of the various discussers of these papers have indicated that the perfused body is subject to variations in vasomotor tone due to causes which may be varied, and many of them remain unknown

This slide merely demonstrates an example of the study, to which Dr. Cordell referred, in which the arterial pressure following the onset of perfusion was definitely reduced. Still, during perfusion, this pressure tended gradually to increase, in spite of the total blood flow remaining constant. Of course, the total peripheral resistance concomitantly increased during this time.

The fact that the blood pressure did decline during perfusion is of concern, and I wonder if it would be appropriate to try to examine these data that have been presented today to see how they influence our selection of an optimal system of perfusion. I think the basic requirement of perfusion is provision of the tissues of the body with the necessary metabolic wants and needs, and it would seem that to accomplish that we must provide an ample flow of blood or ''normal'' blood flow to the capillaries of those tissues. The question is: Is it better to control the flow through the capillaries by perfusing at a theoretically given normal rate or by arterial or venous pressure levels, or is it better to perfuse according to the chemical nature of the blood returning to the machine?

We feel that there are ample data to demonstrate that the capillary blood flow is normal as long as the total body perfusion is in the theoretically normal range. Since vasomotor control and tone are so variable, it is better to perfuse at a given rate and disregard changes in pressure than it is to control the rate of perfusion on the basis of pressure levels alone

DR. J. L. ANKENEY, Cleveland, Ohio.—We, too, have been interested in the effect of perfusion upon vascular resistance and have carried out a series of experiments in which arterial pressure and cardiac output (measured by a rotameter) were recorded and vascular resistance calculated before and after a 45 minute period of extracorporeal bypass. In all animals, hypotension followed perfusion and, in each instance, cardiac output was significantly reduced. In those animals perfused at 100 c.c./Kg./min. (high flow), there was no significant change in vascular resistance as a result of perfusion. However, in dogs perfused at 50 c.c./Kg./min. (low flow), the total vascular resistance was significantly reduced.

Therefore, we found hypotension following high flow perfusion is due to a decrease in cardiac output and not to a change in vascular resistance. Hypotension after low flow rates, however, is due not only to decreased cardiac output but also to a decrease in total body vascular resistance. Postperfusion transfusions return cardiac output and pressure to control levels. Therefore, we have found it efficacious to bring all patients off perfusion with a positive blood balance. As a result, hypotension postoperatively has not been a problem and vasodepressors have not been necessary.

DR. MERRILL P. SPENCER, Winston Salem, N. C.—I find myself in considerable agreement with Dr. McGoon's remarks when he indicated that the peripheral resistance can be ignored if you use an adequate flow rate

Our approach to this problem has been to examine the general total body response to perfusion. It is our plan, as I believe Dr. Kittle indicated, to study regional flow in animals, but for this particular presentation we confined ourselves to the total peripheral resistance.

Among the many factors which can influence peripheral resistance, we have the carotid sinus reflex and we have the agents which have been liberated from breakdown of the cells of the body as it is traumatized, to a greater or lesser extent, through the perfusion apparatus.

The carotid sinus reflex itself is a very basic mechanism, and seems to be a good thing to explain most of the results that we and others have shown. This reflex would predict the findings that Read and his co-workers have shown; namely, that as one increases the flow, the total pressure goes up, but it levels off, so that one reaches a level of pressure where there can be a great change in flow in the body with relatively small changes in pressure. This happens to be within the range of normal arterial pressure, and we find that the maintenance of a normal arterial pressure is not a good indication of whether or not the body tissues are adequately perfused. We should maintain a normal perfusion rate in preference to a normal pressure.

Factors involving the local changes must be studied. We know that the coronary bed and the cerebral bed require a normal arterial pressure in order to get an adequate flow. The brain seemingly has no prominent local mechanism to regulate its flow, so certainly it needs a pressure somewhere within normal range. As far as the rest of the body is concerned—the kidney, the liver, the muscle bed—they undoubtedly show the acidosis of low flow conditions and cause a great deal of trouble in the postoperative period.

We shall say in conclusion that we feel that the flow through the total body is extremely important, and this should be maintained at a high level. Certainly other factors should be monitored, such as arterial pressure and pH (to see whether or not we are getting any acidosis). We must find a way of correcting our pH readings readily and rapidly for CO_2 changes.

We believe that the oxygen tension is very important, particularly in the venous blood returning to the heart, but it is our opinion that the total body flow gives the key factor that must be monitored during perfusion.

LIPURIA AND LIPASEMIA AFTER THORACIC SURGICAL PROCEDURES

F. Price Cossman, M.D. (by invitation), Federico Adler, M.D. (by invitation), C. Frederick Kittle, M.D., and Leonard F. Peltier, M.D. (by invitation), Kansas City, Kan.

THE OCCURRENCE of an elevated serum lipase and the presence of urinary fat in certain diseases and after trauma, associated with operations and injuries, has been noted by several investigators.[11, 12, 28, 29] In some instances these findings have been interpreted as indicative of fat embolization.[4, 9, 18, 21] An elevated serum lipase and lipuria have been demonstrated to occur after fractures,[22] after various orthopedic and soft tissue procedures,[3, 20, 24] in patients with diabetic glomerulosclerosis,[13] and in acute pancreatitis.[15]

Robb-Smith[25] reviewed 789 accidents in which 125 deaths occurred. He was the first to emphasize the importance of large fat globules in the serum of patients dying with fat embolism, although this had been noted previously by others.[35, 36, 37]

Peltier[23] effectively demonstrated the value of a tourniquet in operations upon bone to prevent fat droplets from entering the systemic circulation. On the basis of experimental and clinical data he advised application of a tourniquet in operative procedures involving the bone in order to decrease fat embolism.

Bryans and Eiseman[3] studied 130 patients undergoing various surgical procedures. Sixty-seven of these had had operations involving the soft tissues. Fifty-one of these operations were classed as major procedures; 24 of the patients had postoperative fat globules in the serum. Sixteen were minor procedures; 3 patients had postoperative fat globules. In 37 patients undergoing orthopedic procedures, the incidence of fat globulinemia in 15 major operations was 66.6 per cent (10 patients) and in 22 minor operations was 22.7 per cent (5 patients). They concluded that fat globulinemia is correlated with the degree of operative trauma. In 5 dogs, they fractured the femur of each leg individually and then examined the serum for fat globules after each fracture. In each animal at least one examination showed fat globules in the

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serum, but in 9 of the 20 analyses no globules were noted. They believed that if the origin of the fat globules were from the fracture sites, a higher incidence of globules would be expected.

In an analysis of 75 orthopedic patients, Peltier and Lai[24] found 16 of them with a significantly elevated serum lipase. Twenty of these patients had had elective orthopedic procedures, 48 sustained fractures of one bone, and 7 sustained multiple fractures. No patient with a minor bone injury or with injuries limited to the soft tissue had an elevated serum lipase.

McKeown[19] studied the surgical specimens from 17 patients after lobectomy or pneumonectomy and the lung biopsies of 24 patients having mitral valvotomy. In 10 of the 17 resected lung specimens and in 4 of the 24 lung biopsies, she found fat emboli in the lung. In 2 of the patients, bone marrow emboli were found within the pulmonary vessels. She believed these to be incidental findings and of no clinical significance.

Schmidt[27] has reported a patient with atrial septal defect and anomalous pulmonary venous return who developed symptoms of embolism on the third postoperative day following an exploratory pericardiotomy. The patient died on the fifth postoperative day from bone marrow and fat embolism to the lungs.

Because of our interest in the problem of fat embolism, we should like to present our study of hyperlipasemia and lipuria following various types of thoracotomies, including those with extracorporeal circulation. A series of patients undergoing other surgical procedures is used for comparison. The data include 110 patients, of whom 38 had thoracotomy, 19 utilizing extracorporeal circulation; 32 with either laparotomy or major surgical procedures on soft tissues; and 40 with operative procedures involving fresh skeletal trauma.

METHODS

Samples of the patients' blood and urine were obtained on the day prior to operation and on succeeding days up to the eighth postoperative day. Immediately after obtaining the blood it was transferred to centrifuge tubes, allowed to clot, and centrifuged with subsequent removal of the serum. The urine in most instances was collected from patients after insertion of an indwelling catheter. Samples were collected in volumetric flasks previously washed carefully to remove all traces of fatty substances.

Serum lipase was determined by the method of Cherry and Crandall,[5] as modified by Comfort and Osterberg.[6] This consists essentially of incubating 1.0 ml. of serum with a buffered olive oil emulsion at 37° C. for 24 hours. The free fatty acids released by hydrolysis are then titrated to an end point with 0.5N sodium hydroxide. Results are reported in milliliters of 0.5N sodium hydroxide. The mean serum lipase by this method in our laboratory in 100 normal individuals was 0.37, with a standard deviation of 0.26.

Lipuria was measured by the method of Scuderi.[31] The meniscus of urine in the volumetric flask was skimmed with a 3 mm. platinum loop and its contents smeared on a glass slide. After the slide had been permitted to dry, it was covered with several drops of a saturated solution of Sudan III and 70 per

TABLE I. PATIENTS UNDERGOING THORACOTOMY WITH EXTRACORPOREAL CIRCULATION*

PATIENT	AGE (YEARS)	HEIGHT (INCHES)	WEIGHT (POUNDS)	AREA (M.$_2$)	DIAGNOSIS	PROCEDURE	INCISION	DURATION OF BYPASS (MIN.)
PV	13	50	52.2	0.92	Trilogy of Fallot	Pulmonary valvotomy	Sternal splitting	55
DA	7	49	44.6	0.85	V. S. D.	Closure V. S. D.	Sternal splitting	13
MD	47	61.5	136.4	1.61	A. S.	Aortic valvotomy	Sternal splitting	25
LG	37	67.5	159.9	1.84	A. S. D.	Closure A. S. D.	Transverse thoracotomy	36
EH	13	62	105.5	1.45	V. S. D.	Closure V. S. D.	Sternal splitting	44
JM	5	44	40.6	0.75	V. S. D.	Closure V. S. D.	Sternal splitting	19
DG	5	42	37.2	0.70	V. S. D.	Closure V. S. D.	Sternal splitting	15
JW	27	65	106.3	1.51	M. I.	Mitral repair	Transverse thoracotomy	43
JT	3	33.8	23.1	0.49	V. S. D.	Closure V. S. D.	Sternal splitting	22
PM	13	60.5	85.0	1.30	P. S.	Pulmonary valvotomy	Sternal splitting	55
JD	8	47.5	49.3	0.87	V. S. D.	Closure V. S. D.	Sternal splitting	47
JR	12	58	104.8	1.38	A. S.	Aortic valvotomy	Sternal splitting	21
JM	5	44	40.6	0.75	V. S. D.	Closure A. S. D.	Sternal splitting	19
PP	25	71.5	184.6	2.03	A. S.	Aortic valvotomy	Sternal splitting	40
KD	6	43	35.8	0.70	A. S. D.	Closure A. S. D.	Sternal splitting	37
JJ	7	45.2	40.7	0.77	A. S.	Aortic valvotomy	Sternal splitting	21
JC	6	47	49.3	0.86	P. S.	Pulmonary valvotomy	Sternal splitting	39
MM	9	51	54.4	0.95	A. S.	Aortic valvotomy	Sternal splitting	32
WR	53	69.3	145.9	1.81	A. S.	Aortic valvotomy	Sternal splitting	33

**Legend:* V.S.D. = ventricular septal defect; A.S. = aortic stenosis; A.S.D. = atrial septal defect; M.I. = mitral insufficiency; P.S. = pulmonary stenosis.

cent alcohol. The slide was covered with a cover slip and immediately examined microscopically. The urine also was examined microscopically by the method of Adler, Peltier, and Lai.[1] This consists of a staining technique utilizing Nile blue sulfate as a selective dye. Five drops of this staining solution are layered on the surface of urine in the volumetric flask. After 2 minutes, five drops of ether are added. Following evaporation of the ether, the walls of the flask are examined. If fat globules are present, small drops of pink-to-red color will be precipitated on the walls of the flask above the meniscus.

RESULTS

In the 19 patients who had a thoracotomy with extracorporeal circulation, 9 were males, 10 were females, and their average age was 15.9 years. In 17 patients, a sternal splitting incision was used, and, in 2, an intercostal incision (Table I). Seven patients had a ventricular septal defect, 6 aortic stenosis, 2 atrial septal defect, 2 pulmonary stenosis, 1 mitral insufficiency, and 1 tetralogy of Fallot. Preoperatively (Table II), the mean serum lipase in this group was 0.40 ml. with a standard deviation of 0.20; 3 patients had urine positive for fat. Postoperatively, the mean value for serum lipase on the first postoperative day was 0.48 with a standard deviation of 0.28, on the second day 0.65 with a standard deviation of 0.71, on the third day 0.95 with a standard deviation of 0.70, on the fourth day 0.98 with a standard deviation of 0.71, and on the fifth day 0.92 with a standard deviation of 0.67. Lipuria was found in 9 of the 17 patients on the first postoperative day, 8 of 17 patients on the second day, 9 of 18 patients on the third day, 8 of 17 patients on the fourth day, and 4 of 16 patients on the fifth day.

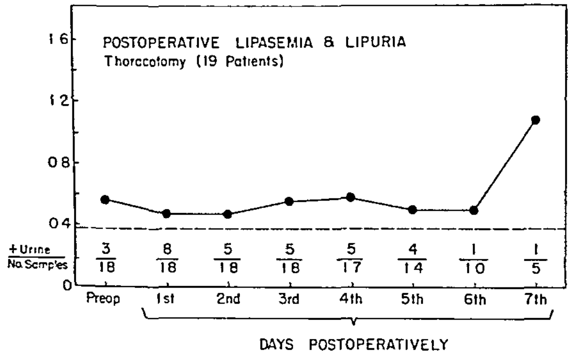

Fig. 1.

All patients undergoing thoracotomy without extracorporeal circulation were adults. This group was composed of 7 males and 12 females. Preoperatively (Table III), mean serum lipase was 0.56 ml. (standard deviation 0.47). Lipuria was found in 2 patients before operation. The mean value for serum lipase was 0.47 ml. (standard deviation 0.32) on the first postoperative day, 0.47 ml. (standard deviation 0.33) on the second day, 0.56 ml. (standard deviation 0.41) on the third day, 0.58 ml. (standard deviation 0.57) on the

TABLE II. LIPASEMIA AND LIPURIA IN PATIENTS IN WHOM EXTRACORPOREAL CIRCULATION WAS USED*

PATIENT	PREOP.		DAYS POSTOPERATIVELY															
			1ST		2ND		3RD		4TH		5TH		6TH		7TH		8TH	
	B	U	B	U	B	U	B	U	B	U	B	U	B	U	B	U	B	U
PV	0.76	–	1.04	+		–	1.55	–	2.73	+	2.95	–	2.55	–				
DA				++		+	0.95	+	1.15	–		–						
MO			0.85	–	2.43	+	2.81	+		+		+		+		+		
LG				+	0.28	+	1.60	+	1.35	+	0.89	+	2.79	+	2.56	+		
EH	0.31			+		+	0.17	+	0.51	+		+	0.71	+	0.43	+		
JM	0.33			+		+	1.08	+	0.29	+	0.60	–		–				
DG	0.37		0.07	–	2.19	–	1.62	–	1.62	–	1.27	–	1.17	–				
JW	0.49		0.22	+	0.66		1.25	+	2.31	+	1.47		1.09	+	2.56	+	2.74	+
JT	0.10		0.49		0.69		0.92		0.58		0.32							
PM			0.37	+	0.26	–		–	0.22	–	0.69	–	0.61	–	0.22	–		
JD	0.38					–		–		+	0.75	–	0.81	–	0.40	–	0.47	–
JR	0.42	±	0.23	–	0.53	–	0.91	–	1.14	–	0.69	–	0.42	–	0.27	–		
JM	0.28	±	0.91	+	0.20	–	0.30	+	0.36	–	0.43	–	0.47	–				
PP	0.93	+	0.52	–	0.45	–	0.45	+	0.38	–	0.09	–	0.43	–	0.44	–		
KD	0.27	–	0.38	–	0.00	+	0.00	–	0.45	–	0.10	–	0.23	–	0.16	–		
JJ	0.40	–	0.52	±	0.48	±	0.58	+	1.16	+	1.34	+	1.26	+				
JC	0.34	–	0.47	–	0.20	–	0.25	–	0.58	–	1.00	–	1.16	–	1.40	–		
MM	0.14	–	0.12	–	0.15	–	0.26	–	0.48	–	0.74	–	1.31	–	1.94	–	1.31	–
WR	0.47	–	0.49	–	0.62	±	1.50	–	1.34		1.40							
Mean	0.40		0.48		0.65		0.95		0.98		0.92		1.07		1.04		1.50	
S. D.	0.20		0.28		0.71		0.70		0.71		0.67		0.74		0.94		0.97	

*B = blood; U = urine.

TABLE III. LIPASEMIA AND LIPURIA POSTOPERATIVELY IN PATIENTS UNDERGOING THORACOTOMIES WITHOUT EXTRACORPOREAL CIRCULATION*

PATIENT	PREOP.		DAYS POSTOPERATIVELY															
			1ST		2ND		3RD		4TH		5TH		6TH		7TH		8TH	
	B	U	B	U	B	U	B	U	B	U	B	U	B	U	B	U	B	U
WF	0.08	±	0.12	–	0.16	–	0.28	–	0.14	–	0.36	–	0.73	–				
NS	0.85	–	0.34	±	0.38	++	0.24	–	0.38	–	0.38	–	0.40	–	0.44	–	0.22	–
HB	0.67	–	0.52	–	0.44	–	0.50	–	0.48	–	0.41	–						
LM	0.20	–	0.18	–	0.52	–	0.11	+	0.15	+	0.15	+	0.18	–				
CM	0.32	–	1.02	+	1.23	+	1.49	+	1.97	+								
AS	0.36	–	0.33	++	0.37	–	0.37	+	0.21	–	0.31	–	0.33	–				
DM	0.22	–	0.31	+	0.21	–	0.24	–	0.19	–	0.17	–	0.22	–				
MK	0.37	–	0.50	–	0.34	–	1.27	–	0.49	–	0.80	–						
JW	0.49	–	0.22	±	0.66	±	1.25	+	2.31	+	1.47	+	1.09	+	2.56	+	2.74	+
EJ	0.37	–	0.64	–	0.30	–	0.53	±	0.99	±	0.69	±						
ME	2.31	–	1.27	±	1.09	–	0.78	–	0.68	–	0.69	±						
GN	0.50	–	0.34	–	0.24	–	0.31	–	0.52	–	0.28	–						
GS	0.54	–	0.56	–	0.31	–	0.37	–	0.20	–	0.25	–	0.36	–				
IG	0.87	–	0.54	–	0.77	–	0.56	–	0.54	–	0.76	–	0.77	–	1.08	–		
LH	0.80	–	1.08	–	1.05	±	1.11	–	0.60	±								
MM	0.69	–	0.21	±	0.16	±	0.44	–	0.49									
JS	0.29	–	0.24	±	0.22	–	0.22	–	0.31		0.46	–	0.51	–	0.24	–		
MR	0.32	+	0.42	–	0.33	–	0.40	–	0.29		0.27		0.41					
LM	0.31		0.06		0.09		0.11		0.15		0.05							
Mean	0.56		0.47		0.47		0.56		0.58		0.50		0.50		1.08			
S.D.	0.47		0.32		0.33		0.41		0.57		0.33							

*B = blood; U = urine.

fourth day, and 0.50 ml. (standard deviation 0.33) on the fifth day. Lipuria was found in 8 of 18 patients on the first postoperative day, 5 of 18 patients on the second day, 5 of 18 patients on the third day, 5 of 17 patients on the fourth day, and 4 of 14 patients on the fifth day.

Thirty-two patients undergoing laparotomy (Table IV) were studied for serum lipase levels. These may be considered as having major soft tissue trauma. Preoperatively, the mean serum lipase was 0.59 ml. with a standard deviation of 0.40. The mean serum lipase level was 0.64 ml. with a standard deviation of 1.03 on the first postoperative day, 0.44 ml. with a standard deviation of 0.57 on the second day, 0.54 ml. with a standard deviation of 0.47 on the third day, 0.61 ml. with a standard deviation of 0.45 on the fourth day, and 0.78 ml. with a standard deviation of 0.72 on the fifth day after operation.

TABLE IV. LIPASEMIA IN PATIENTS AFTER ABDOMINAL OPERATIONS AND OTHER PROCEDURES

NAME	PREOP.	DAYS POSTOPERATIVELY						PROCEDURE
		1ST	2ND	3RD	4TH	5TH	6TH	
TE	0.60	0.69	0.56	0.78	1.07	1.19	2.02	Gastrectomy
ET	0.69	0.54	0.67	0.31	0.14	0.36	0.73	A-P resection
JC	0.24	0.33	0.14	0.08	0.10	0.05		Gastrectomy
LE	0.68	0.43	0.53	0.43	0.49			Cholecystectomy
HK	0.41	0.16	0.09	0.18	0.13	0.40		Bilateral herniorrhaphy
JB	0.17	0.27	0.00	0.12	0.13	0.14		Gastrectomy
RG	0.98	0.26	0.29	0.14	0.94	0.23		Cholecystectomy
BR	0.47	0.17	0.04	0.46	0.75	0.83		Colectomy
EB	0.27	0.20	0.54	0.93	0.90	1.15		Cholecystectomy
CR	1.49	1.54	0.33	1.07	1.14	1.11		Exploratory laparotomy
KM	0.47	0.57	2.53	1.02	1.20	2.04		Splenectomy
AM	0.11	0.09	0.40	0.68	1.20	2.71		Cholecystectomy
RB	1.64	1.05	0.09	0.09	0.22	0.33		Exploratory laparotomy
CO	0.73	0.59	0.25	0.51	0.63	1.29		Colectomy
RW	0.88	0.95	2.17	2.14	1.46			Colectomy
DS	0.55	0.26	0.23	0.72	0.39			Splenectomy
ND	0.29	0.08	0.62	0.30	0.29	0.46		Colectomy
GP	0.38	0.42	0.00	0.15	0.29	0.73		Bilateral herniorrhaphy
KM	0.23	0.04	0.18	0.14	0.30	0.30		Splenectomy
AR	0.68	0.86	0.60	0.90	0.82	1.07		Gastrectomy
EE	0.57	0.23	0.05	0.19	0.61			Cholecystectomy
BT	0.36	0.38	0.32	0.52	0.50			Colostomy
RW	0.80	0.46	0.14	0.00	0.03	0.34		Splenectomy
LS	0.10	0.31	0.03	0.00	0.00	0.00		Gastrojejunostomy
HS	1.11	0.45	0.60	0.81	0.82	0.91		Resection of jejunum
AH	0.26	0.10	0.04	0.86	0.00			Cholecystectomy
RD	0.33	0.13	0.00	0.09	0.40	0.13		Pelvic floor repair
OG	0.47	5.91	1.24	1.07	1.05			Exploratory laparotomy
DK	1.63	1.45	0.83	0.87	0.82	0.86		Cholecystojejunostomy
CR	0.43	0.35	0.31	1.32	1.99	2.49	1.57	Gastrojejunostomy
CH	0.13	0.15	0.17	0.16	0.09	0.07		Lumbar sympathectomy
JB	0.76	0.08	0.00	0.42	0.38	0.31		Gastrectomy
Mean	0.59	0.64	0.44	0.54	0.61	0.78		
S.D.	0.40	1.03	0.57	0.47	0.45	0.72		

Forty patients who had orthopedic operations with bone trauma had a mean serum lipase of 0.50 with a standard deviation of 0.32 preoperatively (Table V). Lipuria was found preoperatively in 10 of these patients. The

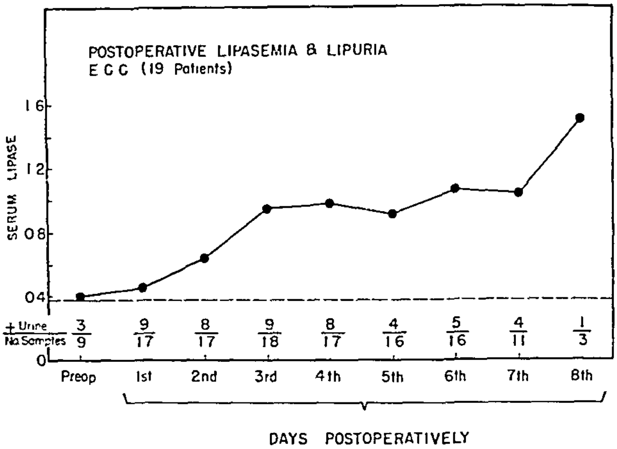

Fig. 2.

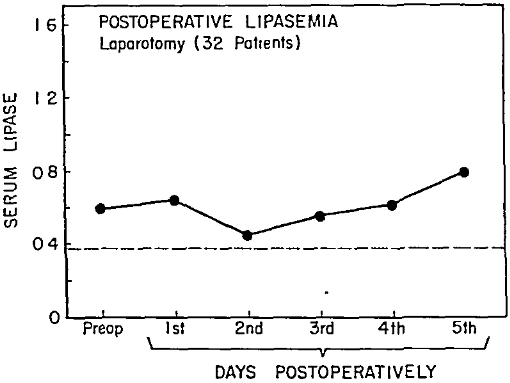

Fig. 3.

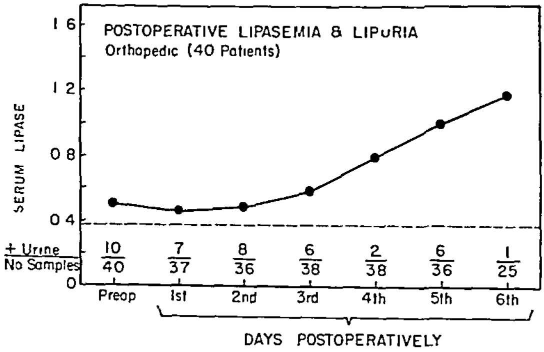

Fig. 4.

TABLE V. LIPASEMIA ASSOCIATED WITH TRAUMA TO BONE*

PATIENT	PREOP.		DAYS POSTOPERATIVELY															
			1ST		2ND		3RD		4TH		5TH		6TH		7TH		8TH	
	B	U	B	U	B	U	B	U	B	U	B	U	B	U	B	U	B	U
IC	0.51	–	0.94	–	0.27	+	0.84	–	0.75	–	1.09	–	0.57	–				
CW	0.75	–	0.24	–	0.46	–	0.69	–	0.81	–	0.85	–	0.70	–				
FM	0.36	–	0.14	–	0.62	–	2.07	–	2.23	–	3.79	–	3.20	–	3.06		228	
GD	1.24	–	1.19	–	0.90	–	0.65	–	1.05	–	0.70	–	1.21	–				
RC	1.15	–	0.73	–	0.77	–	0.72	–	1.30	–	1.68	–	1.71	–				
AM	0.00	–	0.00	+	0.26	–	0.08	–	0.03	–	0.16	–						
KM	0.59	–	0.39	–	0.04	–	0.17	–	0.23	–	0.73	–						
MT	0.41	–	0.52	–	0.52	–	0.66	–	0.60	–	0.48	–	0.45	–				
JU	0.00	–	0.29	–	0.36	–	0.32	–	0.38	–	0.59	–	0.51	–				
EW	0.58	+	0.22	–	0.45	++	0.37	–	0.56	–	1.07	+						
JA	0.29	++	0.01	–	1.10	–	0.09	–	0.00	–								
MH	0.28	–	0.22	–	0.14	–	0.40	–	0.04	–	0.13	–	0.12	–				
MM	0.55	++	0.67	–	0.27	–	0.53	–	1.07	–	1.54	–	2.73	–				
SZ	1.24	–	1.38	–	1.33	–	1.29	–	1.79	–	1.11	–	1.32	–				
LC	0.16	–	1.14		0.31	+	0.31	–	0.45	–	0.37	–	0.72					
FW	0.90	–	0.73	–	0.78		1.00	–	1.21	–	1.99	–	2.31					
LB	0.26	–	0.31		0.51		0.51		0.52		0.58		0.57					
MJ	0.56	+	0.49		0.59	–	0.55	–	0.36	–	0.59	+	0.51	–				
EE	0.12	++	0.22	–	0.38	+	0.84	+	0.46									
CS	0.28	–	0.35	+	0.35	+	0.21	–	0.18	–	0.55	+	0.77	–	0.85	–	1.22	
LJ	0.45	++	0.37	–	0.21	+	0.29	–	0.28	+	0.32	+	0.43					
CT	0.08	–	0.32	–	0.47	–	0.19	–	1.31	–	1.91	–	2.31	–				
EM	0.69	–	0.79	–	0.40	–	0.98	–	1.09	–	1.27	–						
JK	0.71	–	1.35	+	0.80	–	0.54	+	2.44	–	3.44	–	3.62	–				
CW	0.34	++	0.13	–	0.20	–	0.28	++	0.75	++	0.58	+	0.68	–				
AC	0.59	–	0.40	–	0.33	–	0.39	–	0.81	–	0.46	–						
OC	1.01	–	0.60	–	0.57		0.78	–	1.13	–	1.67							
JA	0.52	–	0.12	–	0.24	+	0.26	–	0.35	–	0.51	–						
LM	0.41	–	0.50	–	0.79	–	0.78	+	0.87	–	1.21	–	1.27	–				
JB	0.90	–	0.47	+	0.45	–	0.56	–	0.65	–	1.31	–	0.52	–				
DF	0.13	+	0.30	–	0.87	–	1.36	–	1.77	–	1.10	–	0.97					
CT	0.19	+	0.11	+	0.31	–	0.50	+	1.30	–	1.35	–	1.27	–				
DW	0.70	+	0.44	–	0.34	+	0.19	+	0.17	–	0.22		0.33	+				
AB	0.61	–	0.44	–	0.54		0.46	–	0.60	–	1.01	–	1.03	–				
EE	0.19	–	0.41	+	0.14	–	0.30	–	0.63	–	0.63	+	0.74	–				
CC	0.48	–	0.68	–	0.50	–	1.00	–	0.74	–	0.83	–	1.04	–				
JM	0.40	–	0.19	–	0.38	–	0.51	–	1.00	–	0.68	–						
MC	0.91	–	0.45	–	0.56	–	0.54	–	0.72	–	0.90	–	0.92	–				
MH	0.21	–	0.23	+	0.30	–	0.34		0.12	–	0.36	–	0.44	–				
OG	0.40	–	0.48	–	0.62	–	0.97	–	0.77	–	1.27	–	1.63	–				
Mean	0.50		0.46		0.18		0.59		0.80		1.00		1.16					
S.D.	0.32		0.32		0.26		0.39		0.56		0.77		0.85					

*B — blood, U — urine

mean serum lipase was 0.46 ml. (standard deviation 0.32) on the first postoperative day, 0.48 ml. (standard deviation 0.26) on the second day, 0.59 ml. (standard deviation 0.39) on the third day, 0.80 ml. (standard deviation 0.57) on the fourth day, and 1.00 ml. (standard deviation 0.77) on the fifth day after operation.

DISCUSSION

Parenchymatous embolism is an ubiquitous and protean manifestation of trauma. The association of such embolism with cardiac or thoracic operations may seem tenuous but deserves consideration. This study of lipasemia and lipuria was carried out because of our interest and the observation that fat embolism has been noted in patients who die soon after cardiac operations.[29] In our hands, elevation of the serum lipase and demonstration of lipuria have been the most valuable laboratory methods in the diagnosis of fat emboli in surgical patients.

In our group of patients, the incidence of lipuria was widespread and without significance. It appears that there is a marked elevation in the serum lipase levels, reaching the peak after the third postoperative day, in patients with thoracotomy and extracorporeal circulation and in those with trauma to the bone.

The factor of bone trauma must be considered in both groups since, in all but 2 of the 19 patients with thoracotomy and extracorporeal circulation, a sternal splitting incision was made. However, in the two exceptions, elevations of the serum lipase levels also occurred. This attracts attention to other possibilities.

Haymaker[14] and Gersh[10] and their associates have shown that fat embolism appears in patients and animals in whom there has been a sudden drop (by decompression) in the partial pressure of nitrogen in the blood. This was believed to be due to rupture of fat cells by bubbles of escaping nitrogen dissolved in the fat under previous ambient pressure. We have found that by suddenly shifting the composition of the atmosphere from 95 per cent nitrogen and 5 per cent oxygen or from 80 per cent nitrogen and 20 per cent oxygen to 100 per cent oxygen, rats, in a period of 10 minutes, developed pulmonary fat embolism.[7] It appears feasible, therefore, that sudden changes in local fatty tissue pressure of nitrogen may result in the phenomena described by Gersh and his co-workers.

The source of fat in both circumstances may be local trauma to fat cells in the sternum or diffuse trauma to fat cells because of the rapid variation in pN_2. Swank[34] and Lehman[16] and others have shown experimentally that fat globules in the circulating blood as a metabolic lipemia may agglomerate to form fat emboli. Recently we have repeated their experiments but have failed to confirm their findings. On this basis, we believe that the conclusion of Scott and his co-workers,[30] regarding the source of embolic fat from blood lipids, is unwarranted.

Lipase is known to be present in or secreted by the stomach, pancreas, liver, lung, and leukocytes, as well as many other organs and tissues.[8, 32] In these patients we believe the source of the elevated lipase most probably to be the lung. Lipase from other organs and tissues is not secreted in sufficient quantity to elevate blood levels, while lung lipase is secreted in response to the presence of emboli of neutral fat to the lung.[21] Under normal circumstances there is no relationship between metabolic or alimentary lipemia and an elevated serum lipase. However, in patients with chronic hyperlipemia the serum lipase may be elevated.[32] LeVeen and his associates[17] recently have shown that no appreciable change in blood lipid levels occurs in patients postoperatively.

In hyperlipasemia after extracorporeal circulation, some consideration should be given to the lipase changes after administration of heparin. Lipase activity can be detected in the plasma shortly after intravenous injection of heparin.[33] The addition of heparin to normal plasma in vitro does not initiate lipase action in the plasma or a lipid emulsion added to normal plasma which contains heparin is not cleared.[2] These observations suggest that the lipase, or some component necessary for its action, is released into the plasma by the injected heparin from some immediately accessible site. It has been suggested that the essential component is distributed generally in the walls of blood vessels in the body.[26] In our patients the failure of the serum lipase to become elevated until the fifth day minimizes the importance of this factor.

CONCLUSIONS

1. Determinations of serum lipase and urinary fat have been made in 110 patients undergoing a variety of surgical procedures. Nineteen had thoracotomy using extracorporeal circulation; 19 had thoracotomy alone; 32 had laparotomy for major surgical procedures involving soft tissue; and 40 had orthopedic operations with skeletal trauma.

2. Lipuria was noted occasionally in patients both preoperatively and postoperatively; because of its sporadic occurrence, no significance is ascribed to it.

3. Serum lipase was significantly elevated in patients with thoracotomy, most of whom had had sternal splitting incisions, and in patients undergoing orthopedic operations with bone trauma.

4. Possible explanations for this hyperlipasemia are suggested.

5. No clinical significance of the elevated serum lipase or lipuria has been noted.

REFERENCES

1. Adler, F., Peltier, L. F., and Lai, S. P.: Fat Embolism: The Determination of Fat in the Urine by Microscopic and Macroscopic Methods, Surgery 47: 959, 1960.
2. Anderson, N. G., and Fawcett, B.: An Antichylomicromemic Substance Produced by Heparin Injection, Proc. Soc. Exper. Biol. & Med. 74: 768-771, 1950.
3. Bryans, W., and Eiseman, B.: The Incidence of Fat Globulinemia Following Soft Tissue and Orthopedic Operations, Surgical Forum, 1954, American College of Surgeons, Philadelphia, 1955, W. B. Saunders Company.
4. Caldwell, G. T., and Huber, H. L.: Fat Embolism Following Trauma to Bones, Surg. Gynec. & Obst. 25: 650-663, 1917.

5. Cherry, I. S., and Crandall, M. A., Jr.: The Specificity of Pancreatic Lipase: Its Appearance in the Blood After Pancreatic Injury, Am. J. Physiol. 100: 266-273, 1932.
6. Comfort, M. W., and Osterberg, A. E.: The Value of Determination of the Concentration of Serum Amylase and Serum Lipase in the Diagnosis of Disease of the Pancreas, Proc. Staff Meet. Mayo Clin. 15: 427-432, 1940.
7. Davies, J., and Peltier, L. F.: Fat Embolism: The Failure of Deep Ether Anesthesia During Alimentary Lipemia to Provoke Fat Embolism in Dogs. (In press.)
8. Deuel, H. J.: The Lipids, Their Chemistry and Biochemistry, New York, 1955, Interscience Publishers, Inc., vol. 2.
9. DuToit, J.: Traumatic Fat Embolism, South African M. J. 23: 1062-1065, 1949.
10. Gersh, I., Hawkinson, G. E., and Rathbun, E. N.: Tissue and Vascular Bubbles After Decompression From High Pressure Atmospheres. Correlation of Specific Gravity With Morphological Changes, J. Cell. Physiol. 24: 35-70, 1944.
11. Glas, W. W., Grekin, T. D., Davis, H. L., and Musselman, M. M.: An Experimental Study of the Etiology of Fat Embolism, Am. J. Surg. 91: 471-480, 1956.
12. Glas, W. W., Musselman, M. M., and Davis, H. L.: The Source of Fat in Fat Embolism, Arch. Surg. 71: 600-604, 1955.
13. Hartcroft, W. S.: Fat Emboli in Glomerular Capillaries of Choline Deficient Rats and Patients With Diabetic Glomerulosclerosis, Am. J. Path. 36: 381-397, 1955.
14. Haymaker, W., and Davison, C.: Fatalities Resulting From Exposure to Simulated High Altitudes in Decompression Chambers, J. Neuropath. 9: 29-59, 1950.
15. Johnson, S. R.: Investigations With Regard to the Pathogenesis of So-called Fat Embolism, Ann. Surg. 144: 145-151, 1956.
16. Lehman, E. P., and Moore, R. M.: Fat Embolism, Including Experimental Production Without Trauma, A. M. A. Arch. Surg. 14: 621-622, 1957.
17. LaVeen, H. H., Hidockenko, K., and Giordano, P.: Circulating Lipids in Surgical Patients, A. M. A. Arch. Surg. 80: 698-704, 1960.
18. Love, J., and Stryker, W. S.: Fat Embolism: A Problem of Increasing Importance to the Orthopedist and the Internist, Ann. Int. Med. 46: 342-351, 1957.
19. McKeown, F.: Fat Embolism in Thoracic Operations, Brit. M. J. 1: 150-151, 1955.
20. Peltier, L. F.: Fat Embolisms Following Intramedullary Nailing, Surgery 32: 719-722, 1952.
21. Peltier, L. F.: The Mechanics of Parenchymatous Embolism, Surg. Gynec. & Obst. 100: 612-618, 1955.
22. Peltier, L. F.: Fat Embolism: The Prophylactic Value of the Use of the Tourniquet, J. Bone & Joint Surg. 38A: 835-840, 1956.
23. Peltier, L. F.: An Appraisal of the Problem of Fat Embolism, Surg. Gynec. & Obst. 104: 313-324, 1958.
24. Peltier, L. F., and Lai, S. P.: Fat Embolus: Changes in the Serum Lipase Levels of Patients After Fresh Fractures and Orthopedic Operations, Surgical Forum, American College of Surgeons, Philadelphia, 1960, W. B. Saunders Company, vol. 9.
25. Robb-Smith, A. H. T.: Pulmonary Fat Embolism, Lancet 1: 135-141, 1941.
26. Robinson, D. S., and Harris, P. M.: The Production of Lipolytic Activity in the Circulation of the Hind Limb in Response to Heparin, Quart. J. Exper. Physiol. 44: 80-90, 1959.
27. Schmidt, J. H.: Fatal Bone Marrow Embolism Following Thoracotomy, Am. J. Surg. 95: 94-101, 1958.
28. Schuttemeyer, W.: Klinische Auswertungen der Lipasebestimmungen zur Diagnose der Fettembolie, Arch klin. chir. 270: 50-53, 1951.
29. Schuttemeyer, W., and Flach, A.: Neue Untersuchungsmethode zur Diagnose der Fettembolie, Chirurg 21: 289-292, 1950.
30. Scott, H. W., Jr., Adams, J. E., Owens, G., Mann, G., Headrick, J. R., and Munoz, A.: Experimental Evaluation of Pluronic F^{68} as a Method of Diminishing Systemic Fat Emboli Resulting From Prolonged Cardiopulmonary Bypass, Surgical Forum, 1959, American College of Surgeons, Philadelphia, 1960, W. B. Saunders Company.
31. Scuderi, C. S.: Fat Embolism: A Clinical and Experimental Study, Surg. Gynec. & Obst. 72: 732-746, 1941.
32. Sumner, J. B., and Myrback, K.: The Enzymes: Chemistry and Mechanism of Action, New York, 1950, Academic Press Inc.
33. Swank, R. L.: Changes in Blood Produced by a Fat Meal and by Intravenous Heparin, Am. J. Physiol. 164: 798-811, 1951.
34. Swank, R. L., and Dugger, G. S.: Fat Embolism: A Clinical and Experimental Study of Mechanism Involved, Surg. Gynec. & Obst. 98: 641-652, 1954.
35. Vance, B. M.: The Significance of Fat Embolism, Arch. Surg. 23: 426-465, 1931.
36. Warthin, A. S.: A Critical Evaluation of Traumatic Lipemia and Fatty Embolism, Internat. Clin. 4: 171-227, 1913.
37. Wright, R. B.: Fat Embolism, Ann. Surg. 96: 75-84, 1932.

DISCUSSION

DR. LEWIS H. BOSHER, Richmond, Va.—Dr. William H. Scott 2 years ago called attention to the importance of fat mobilization during extracorporeal circulation, and, as a result of his work, we asked Dr. John Forbes in our Biochemical Department to make some fat studies for us.

On seven prolonged perfusions, Dr. Forbes studied the cholesterol and neutral fats in patients about 5 minutes after initiating the perfusion, and at the end of perfusion [slide]—these figures represent the average of seven prolonged perfusions, averaging 1 hour and 54 minutes, and in the first row you have the values seen for total cholesterol and neutral fats in milligrams per cent. At the end of the perfusion there is no change in these values. We concluded there was no evidence for mobilization of fat during the perfusion. In addition, Dr. Forbes centrifuged the serum at 20,000 g; this technique also failed to show any change in the values.

It's hard, I think, to interpret these figures, and I don't know how they fit into the results that have just been reported, but I present them for what they are worth.

DR. JAMES V. MALONEY, Los Angeles, Calif.—I particularly enjoyed this paper by Dr. Cossman, Dr. Adler, and Dr. Kittle for two reasons. First, the paper has the same scientific exactitude as the paper they presented 2 years ago; and now they are showing, perhaps, that similar endogenous materials may exist. Second, I enjoyed it because we can support it with some experiments from our laboratory.

Drs. Fonkalsrud, Miller, and Latta in our laboratory studied the autopsy material in 40 patients who had undergone surgical procedures with the use of the pump-oxygenator and who died in our hospital during the past 5 years. Interestingly enough, in between 55 and 80 per cent of the cases, extensive fat embolism could be found, depending on which organ was examined. We were at that time quite excited by the clinical significance of these findings until we ran control observations. Much to our surprise, 63 per cent of the routine autopsy specimens in the surgical service were found to have extensive fat embolism. Strangely enough, the patients who come from medical wards rarely have fat embolism demonstrated in their tissues at autopsy.

We certainly would agree with Dr. Cossman's concluding statement, that we are much in the dark as to the exact clinical significance of these findings. Nevertheless, it certainly does appear that there are extensive changes in the lipid system of the body under extracorporeal circulation.

DR. KITTLE (Closing).—I wish to thank Dr. Bosher and Dr. Maloney for their remarks.

I can't explain the discrepancy between data presented by Dr. Bosher and our finding of hyperlipasemia. Unquestionably in many patients there is a significantly and definitely elevated serum lipase. What this means, I think, yet remains to be unraveled.

The finding of Dr. Maloney about fat emboli in autopsy material correlates very well with a previous study by Vance which shows a high incidence of microscopic fat emboli in routine autopsies.

THE SURGICAL TREATMENT OF EMPHYSEMATOUS BLEBS AND LOCALIZED VESICULAR AND BULLOUS EMPHYSEMA

Analysis of 50 Cases

James M. Head, M.D. (by invitation), Louis R. Head, M.D. (by invitation), Theodore R. Hudson, M.D., and Jerome R. Head, M.D., Chicago, Ill.*

THE SURGICAL treatment of emphysema is one of the most recent, most difficult, and most challenging fields in thoracic surgery. The numerous publications in the recent literature[1-19] attest to the newness of this therapeutic approach. It is difficult chiefly in its indications and challenging because the incidence of this crippling and eventually fatal disease seems to be increasing as rapidly as is that of bronchogenic carcinoma.

The present paper is a report of the immediate and late results in 31 patients operated upon for emphysematous blebs and 19 patients operated upon for localized vesicular and bullous emphysema. It is therefore divided into two parts.

EMPHYSEMATOUS BLEBS

Discussion.—Emphysematous blebs (Fig. 1) are blisters beneath the visceral pleura. They are to be distinguished from lung cysts, which are congenital, and from localized areas of extreme vesicular and bullous emphysema.[20, 21] The latter result from the breakdown of interalveolar septa. The large blebs (Fig. 2) with which we are to deal are probably of different etiology from the small apical blebs which so frequently cause spontaneous pneumothorax. The latter are probably caused by the apical scarring resulting from the usual apical deposits of the primary tuberculous infection. The former are usually associated with pulmonary emphysema, although as Laennec[22] pointed out, they may develop in otherwise healthy lungs.

On their outer surface these large blebs are covered with a thin layer of visceral pleura. When viewed from within with the thoracoscope during life, the lung surface has on it many alveolar openings which open during expiration and close during inspiration.[23, 24] This seemingly paradoxical phenomenon explains why they become distended after bouts of coughing and why, over the years, they increase steadily in size.

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Blebs are usually multiple and bilateral, but may be single and unilateral. They may be truly gigantic (Fig. 3) and occupy most of the space in one or both pleural cavities. Korol,[25] Peabody, Katz, and Davis,[26] and West and Van Schoonhoven[27] have demonstrated that they predispose to bronchogenic carcinoma (Fig. 4). If they become infected so that fluid forms in them, the alveloar openings into them are closed, the air is absorbed, and they disappear.[28]

The surgical indications for the removal of large emphysematous blebs are obvious. Not only do they collapse the functioning lung in the same manner as does spontaneous pneumothorax, but they also tend to enlarge, and they predispose to carcinoma. In 1943 we first operated upon a man who had multiple large blebs at the apices of both lungs. After the operation, persistent air leaks

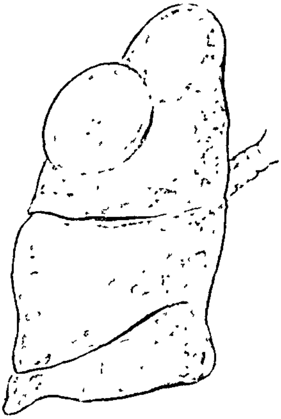

Fig. 1.—Schematic representation of an emphysematous bleb lying within the right upper lobe. Such blebs are to be distinguished from congenital lung cysts and from localized areas of extreme vesicular and bullous emphysema

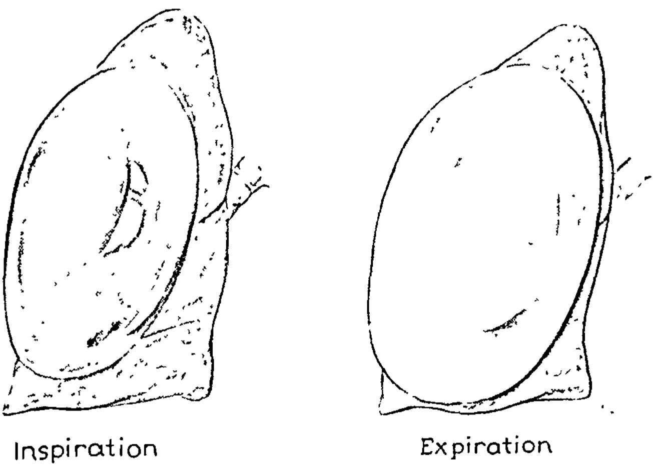

Fig. 2.—These large emphysematous blebs are covered with a thin layer of visceral pleura. The inner lung surface has on it many alveolar openings which open on expiration and close on *inspiration.* This paradoxical phenomenon causes them to enlarge during the expiratory phase of the cycle (coughing). During the [illegible] of the cycle, they tend to remain enlarged and distended for the pressu [illegible] uch greater than the negative intrapleural pressure that occurs during [illegible] xplains why they become so distended after bouts of coughing and why, [illegible] increase steadily in size.

made it difficult to re-expand the lung and the patient almost died of retained secretions. He recovered, however, and his vital capacity was increased from 1,200 c.c. to 1,800 c.c.

In the early 1940's, at about the same time that the aforementioned patient was seen, we were using Monaldi's intracavitary suction to close tuberculous excavations It occurred to us that this procedure might prove a simple and safe way of closing blebs It did, and in 1948 we reported before this Society 8 cases in which this had been used successfully.[24] Today we believe

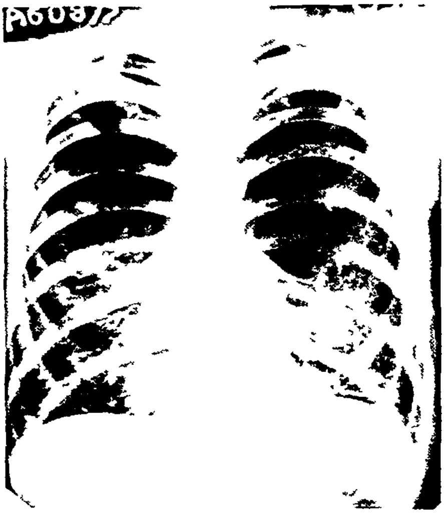

Fig 3—Roentgenogram which shows bilateral multiple gigantic blebs which occupy most of both pleural cavities

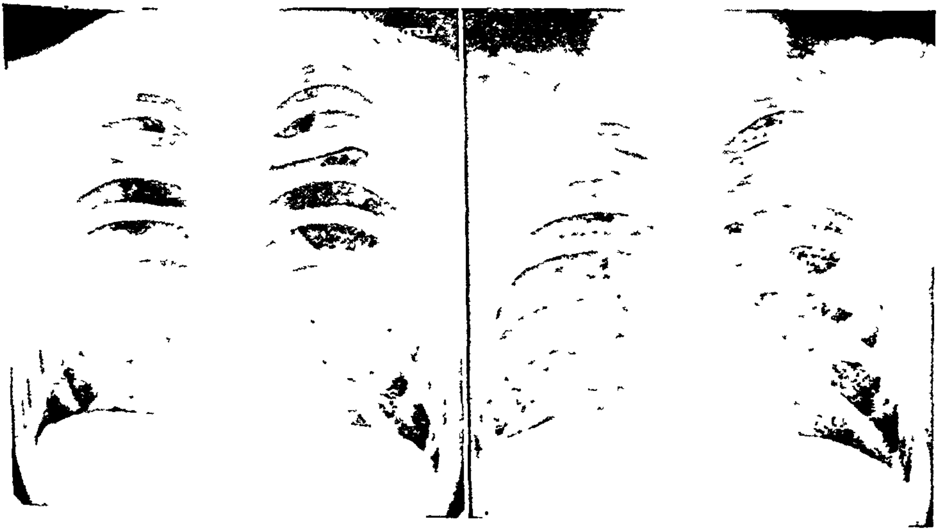

Fig 4—Roentgenograms of a 36-year-old white man who developed a bronchogenic carcinoma at the site of a previous bleb collapsed by Monaldi suction 2 years earlier

that the open operation is preferable in all patients, save those who are extremely feeble and dyspneic, and perhaps even in these patients with the aid of the mechanical respirator. In most cases the blebs are multiple and today the refined techniques of open operation, the improvements in postoperative bronchial toilet, and the use of tracheostomy and the mechanical respirator have made the open operation very safe.

We have divided the cases of emphysematous blebs into two groups: the *first*, those in which, apart from the blebs, the lungs are normal, and the *second*, those in which they are complicated by an underlying generalized emphysema.

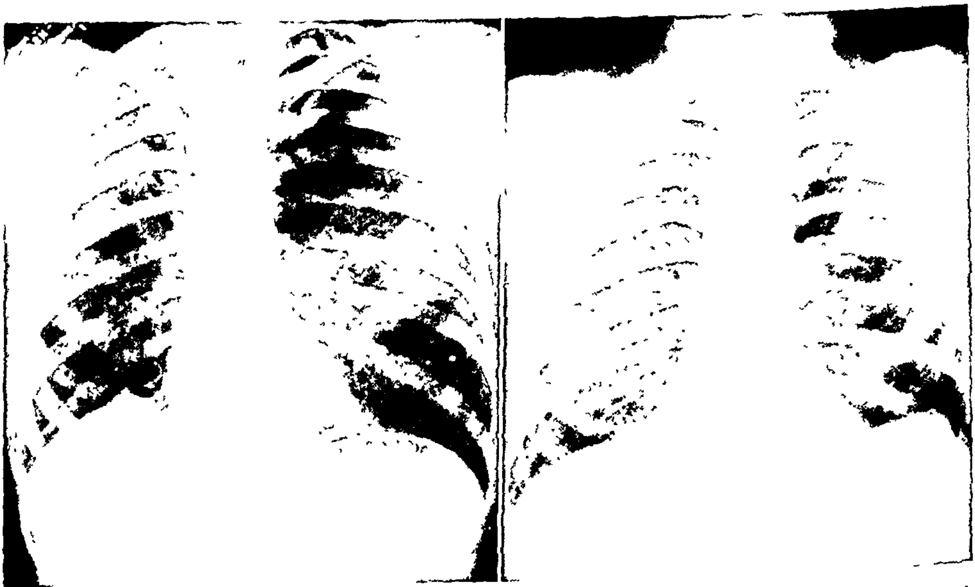

Fig. 5.—Case 1. Pre- and postoperative x-ray studies of a patient with blebs on normal lungs. After a second operation he had normal respiratory function.

Case Reports

CASE 1.—B. S.; CWMH 389270. Fig. 5 shows the pre- and postoperative roentgenograms of a patient with blebs on normal lungs. Before the first operation the patient was markedly short of breath. Since the second operation, which was performed in 1954, he has had normal respiratory function.

CASE 2.—H. S.; CWMH 310423. Fig. 6 shows the pre- and postoperative roentgenograms of a patient with bilateral giant blebs complicated by generalized emphysema. Prior to the operation he was completely incapacitated, even dressing and shaving were too great a tax on his breathing. He could not tolerate respiratory function studies. After the operations, although still dyspneic on moderate exertion, he was sufficiently improved to be able to return to work. However, his dyspnea became gradually worse. At the end of 3 years he was again forced to stop work and 4 years after the operation he died of cor pulmonale.

These typical cases illustrate the essential difference between the two groups. In the uncomplicated cases, removal of the blebs gives both immediate and

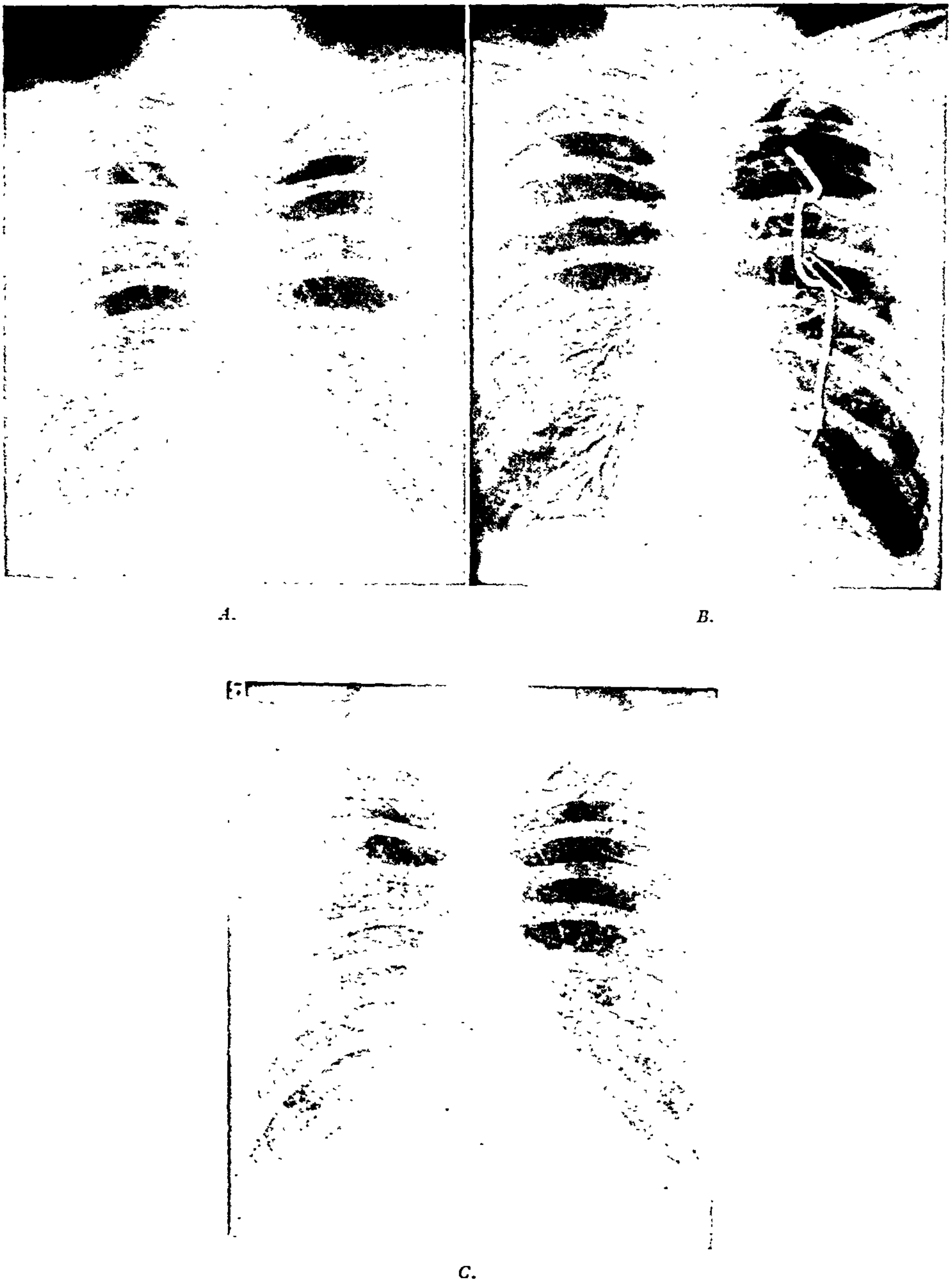

Fig. 6.—Case 2. Pre- and postoperative roentgenograms of a patient with bilateral giant blebs complicated by emphysema. The bleb on the left was collapsed by Monaldi suction. The bleb on the right was resected. The patient died 4 years later of cor pulmonale. He had been working for 3 years prior to his death.

permanent relief. In those complicated by emphysema, the patients are greatly relieved immediately, but the emphysema always progresses and they die of right heart failure.

Operative Mortality and Type of Surgery.—Of the 31 patients operated upon for emphysematous blebs 3 have been lost to follow-up. Sixteen (57 per cent) of the remaining 28 patients (Table I) had blebs on underlying normal lungs, while 12 (43 per cent) had blebs complicated by pulmonary emphysema.

TABLE I. OPERATIVE MORTALITY AND TYPE OF SURGERY IN 28 PATIENTS OPERATED UPON FOR EMPHYSEMATOUS BLEBS

	NO. OF CASES	OPERATIVE MORTALITY	TYPE OF OPERATION		
			MONALDI	MONALDI + RESECTION	RESECTION
Uncomplicated by emphysema	16 (57%)	0 (0%)	4 (25%)	2 (12.5%)	10 (62.5%)
Complicated by emphysema	12 (43%)	0 (0%)	7 (58%)	1 (8%)	4 (34%)
Totals	28 (100%)	0 (0%)	11 (39%)	3 (11%)	14 (50%)

The operative mortality in this group of cases was zero.

Of the 16 patients with pure blebs, 4 (25 per cent) were treated with Monaldi suction, 2 (12.5 per cent) were treated with Monaldi suction plus resection, and 10 (62.5 per cent) were treated by resection alone.

Seven (58 per cent) of the patients with the complication of emphysema were treated with Monaldi suction, 1 (8 per cent) was treated with Monaldi suction plus resection, and 4 (34 per cent) were treated with resection alone.

Results and Long-Term Follow-Up.—All of the patients operated upon for pure emphysematous blebs (Table II) noted excellent immediate results. Only 2 (12 per cent) of these patients are recorded as having poor late results. One of the latter has been followed only for 2 months so that it is too early to determine the late result. However, we have every reason to believe that this patient will have an excellent long-term survival. The second patient died at the end of 2 years from a bronchogenic carcinoma which had arisen at the site of a previous bleb collapsed by Monaldi suction. The patient was asymptomatic with regard to his initial disease at the time of death.

ABLE II. RESULTS AND DURATION OF FOLLOW-UP IN 16 CASES OF BLEBS UNCOMPLICATED BY EMPHYSEMA

IMMEDIATE RESULT		LATE RESULT		DURATION OF FOLLOW-UP					TOTAL	OVER-ALL RESULT	
GOOD	POOR	GOOD	POOR	2 MO	1-2 YR	2-4 YR	8-10 YR	12 YR		EXCELL	POOR
16 (100%)	0 (0%)	14 (88%)	2 (12%)	1 (6.25%)	6 (37.5%)	4 (25%)	2 (12.5%)	3 (18.2%)	16 (100%)	14 (88%)	2 (12%)

The duration of follow-up in this group varies from 2 months to 12 years. The over-all picture in this group of cases, then, is excellent immediate and long-term results.

The immediate effect of surgery noted in the cases of blebs complicated by pulmonary emphysema (Table III) was good in all 12 (100 per cent) cases. Six (50 per cent) of these patients noted good late results, while 6 (50 per cent) noted poor late results. Of those patients classified as showing poor late results, all had a return of their initial symptoms within 2 to 10 months. Two of these are alive with symptoms of progressive emphysema 12 and 36 months after surgery, while 4 died of cor pulmonale 9, 18, and 24 months, postoperatively. The 6 (50 per cent) patients recorded as showing good late results are classified as such only because they did not note a return of their initial symptoms until from 3 to 8 years after treatment. Of these 6 patients, 1 is alive with symptoms of progressive emphysema 7 years later, while 5 died from right heart failure from 4 to 12 years after surgery. The over-all prognosis in this form of the disease is poor in spite of the good immediate result, for all of the patients eventually die of their emphysema.

TABLE III. RESULTS AND DURATION OF FOLLOW-UP IN 12 CASES OF BLEBS COMPLICATED BY EMPHYSEMA

CASE	IMMEDIATE RESULT	LATE RESULT	DURATION OF FOLLOW-UP			OVER-ALL RESULT
			RETURN OF SYMPTOMS	ALIVE WITH SYMPTOMS	DIED	
1. W. M.	Good	Poor	2 mo.	–	9 mo.	Poor
2. A. M.	Good	Poor	6 mo.	–	18 mo.	Poor
3. D. E.	Good	Poor	8 mo.	12 mo.	–	Poor
4. O. R.	Good	Poor	8 mo.	–	24 mo.	Poor
5. T. L.	Good	Poor	10 mo.	36 mo.	–	Poor
6. C. G.	Good	Poor	10 mo.	–	18 mo.	Poor
7. E. A.	Good	Good	3 yr.	7 yr.	–	Poor
8. H. S.	Good	Good	3 yr.	–	4 yr.	Poor
9. R. G.	Good	Good	5 yr.	–	8.5 yr.	Poor
10. W. K.	Good	Good	6 yr.	–	8.5 yr.	Poor
11. J. G.	Good	Good	7 yr.	–	12 yr.	Poor
12. E. M.	Good	Good	8 yr.	–	10 yr.	Poor

LOCALIZED VESICULAR AND BULLOUS EMPHYSEMA

Discussion.—In localized vesicular and bullous emphysema, we are confronted with a more complex problem; not only from the standpoint of the altered physiology and the pathology present, but also from the standpoint of the indications for surgery. The rationale of surgery for generalized vesicular and bullous emphysema is different and more complicated than for emphysematous blebs. In this disease the inelastic lungs are simply too large for the thorax. They are crowded into it. This crowding interferes with the mechanics of respiration and circulation. It forces the diaphragm down and out of function. As Brantigan[29, 30, 31] has pointed out, it contributes to the obstruction of the finer air passages and so to a reduced maximum breathing capacity with bronchial infection, cough, and wheezing. The increased pressure on the great veins and auricles produces a relative cardiac tamponade. The lungs are rarely uniformly involved (Fig 7), and those areas most dilated, most inelastic, and most obstructed compress and put out of function the more elastic and normal lung portions. Operation by resection of the areas most severely involved aims to reduce the size of the lung and so raise the diaphragm, decrease the obstruction of the bronchioles, lessen the pressure on the heart and great veins, and bring the more normal lung portions back into function.

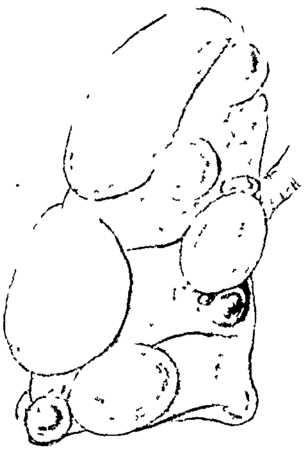

Fig. 7.—In vesicular and bullous emphysema, the lungs are rarely uniformly involved. Those areas most dilated, most inelastic, and most obstructed compress and put out of function the more elastic and normal lung portions. Operation by resection of the areas most severely involved aims to reduce the size of the lung and so to raise the diaphragm, decrease the obstruction of the bronchioles, lessen the pressure on the heart and great veins, and to bring the more normal lung portions back into function.

In his original classical description of emphysema, Laennec[22] pointed out that emphysema rarely involved all lung portions equally—that in nearly all cases some areas were worse than others and that the disease might be limited to one lung, or to one lobe or segment.

In 1951, in a paper read before The Chicago Society of Internal Medicine,[23] we discussed cases of this kind and suggested that there might be relief by surgery. In 1952 we operated upon such a patient and since then have operated upon a total of 19. We have, of course, seen many more cases of emphysema. Most of these patients, however, can be made reasonably functional by medical treatment and/or pneumoperitoneum.

We have selected for operation only those cases in which the roentgenograms revealed that part or parts of the lung were more involved than others. We have not, as Brantigan advises,[29, 30, 31] operated upon patients with generalized disease in order merely to decrease the size of the lungs. While this may be feasible and advisable, we have not dared to do it, feeling that in these cases there was too little normal lung present.

We have chosen to present 3 typical cases to illustrate the indications we have used and the results which can be obtained.

Case Reports

Case 3.—M. L., CWMH 427042 (Fig. 8). A 55-year-old white female secretary was almost completely incapacitated by dyspnea. She was severely dyspneic at complete rest and coughed almost constantly. She had grown progressively worse in spite of medical treatment. The roentgenogram revealed emphysema at the bases of both lungs and what appeared to be a large bleb on the right side. She was too dyspneic to undergo pulmonary function studies. At operation on May 17, 1956, the right middle lobe was tremendously dilated by generalized nonbullous emphysema. The apex of the lower lobe was similarly affected. The middle lobe was removed and the apex of the lower lobe was wedged off. Segmental resections are contraindicated in emphysema.

Following operation the cough and wheezing practically disappeared and 6 weeks after discharge from the hospital she was walking 7 miles a day. She returned to work and is working today, 4 years after the operation. In 1958 she underwent surgery for carcinoma of the colon. Although some cough has returned and dyspnea is gradually increasing, she still has a practical respiratory capacity 4 years after surgery.

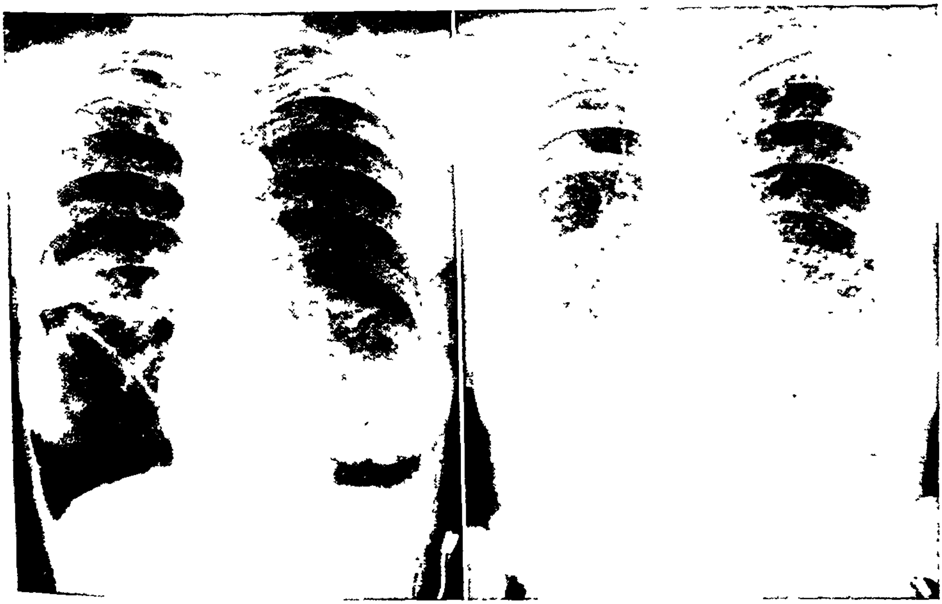

FIG. 8.—Case 3. Pre- and postoperative roentgenogram of a 55-year-old white woman who had a right middle lobectomy and wedge resection of the apex of the lower lobe for localized vesicular (nonbullous) emphysema. Before operation she was almost completely incapacitated. The patient is alive and working 4 years after operation with only minimal symptoms.

CASE 4.—H. McK., CWMH 484538 (Fig. 9). This 51 year-old white male high school teacher had noted progressive dyspnea, cough, and wheezing since 1948. The symptoms had progressed to the point that he was barely able to carry on his teaching responsibilities. The roentgenogram revealed what was believed to be contraction and compression of the left upper lobe by a markedly distended and emphysematous left lower lobe. There was also evidence of bullous emphysema in the right lower lobe area. Pulmonary function studies revealed a maximum breathing capacity (MBC) of 29 per cent of predicted normal, a vital capacity (VC) of 58 per cent of predicted normal, a 3-second timed vital capacity (TVC) of 68, 75, and 92 per cent, a residual lung volume (RLV) of 131 per cent of predicted normal, and a R.V./T.L.V. ratio of 50 per cent (30 to 35 per cent normal).

At thoracotomy on Oct. 23, 1958, a large emphysematous portion of lung was seen filling the entire left pleural space. This was found to arise only from the superior segment of the lower lobe. It was removed in wedge fashion along with two smaller areas of similarly involved lung from the lower lobe.

When last seen in April of 1960 the patient was fully engaged in his teaching profession, traveling to educational conventions, and performing his own yard and garden chores with minimal difficulty. Pulmonary function studies on April 27, 1960, revealed a MBC of 47 per cent of predicted normal, a VC of 100 per cent of predicted normal, a 3-second TVC of 40, 50, and 60 per cent, a RLV of 116 per cent of predicted normal, and a R.V./T.L.V. ratio of 34 per cent (30 to 35 per cent normal). We have never seen a patient more pleased with the results of surgery. It has been our experience that frequently the objective function studies do not reveal the excellent subjective clinical improvement noted by the patients.

CASE 5.—F. H., CWMH 484503 (Fig. 10). This 51-year-old white housewife had been bothered by cough, sputum production, dyspnea, and wheezing for 10 to 12 years. For the past 2 to 3 years she had noted progressive dyspnea which had become especially severe after an attack of pneumonia 2 to 3 months before admission to the hospital. She was incapacitated to the point where she was unable to do any housework. She had been cyanotic for many years. A roentgenogram revealed generalized emphysema with a very large bleb-like appearing area occupying the entire lower one half of the right pleural cavity. Bronchogram revealed universal bronchiectasis. She was unable to tolerate pulmonary function studies.

On Nov. 19, 1958, a tracheostomy was performed and the patient placed on a mechanical respirator (Mörch). At the time of tracheostomy the patient's blood was almost black in color. With the institution of mechanical respiration the cyanosis disappeared and she was much more comfortable. On Nov. 25, 1958, with respiration being maintained by the mechanical respirator, operation was performed and a tremendously enlarged, emphysematous right middle lobe was found to be compressing the remaining lung portions. The middle lobe was removed and the patient was maintained on the mechanical respirator for several weeks postoperatively. When she resumed her own respiratory activity, she found her breathing much easier and upon returning home she was eventually able to resume her household duties. She remains much improved with regard to her dyspnea, but continues to be bothered by cough and sputum production, secondary to her universal bronchiectasis. When last seen in February of 1960 she was in early right heart failure. This has been controlled temporarily and her cough and sputum production have improved on medical management. Although temporarily much improved by surgery, the eventual outcome of this case is obvious.

Operative Mortality and Type of Surgery.—In the group of 19 cases (Table IV) there were 4 (21 per cent) operative deaths: 1 from right heart failure, 1 from thrombosis of the pulmonary vein, 1 from a Pseudomonas pneumonia, and 1 patient died suddenly 6 days after discharge from the hospital.

TABLE IV. OPERATIVE MORTALITY AND TYPE OF SURGERY IN 19 PATIENTS OPERATED UPON FOR LOCALIZED VESICULAR OR BULLOUS EMPHYSEMA

NO. OF CASES	OPERATIVE MORTALITY	TYPE OF SURGERY		
		MONALDI	MONALDI + RESECTION	RESECTION
19	4 (21%)	1 (5.3%)	2 (10.5%)	16 (84.2%)

One (5.3 per cent) of the patients had been treated by Monaldi's suction alone, 2 (10.5 per cent) were treated by Monaldi suction plus resection, and 16 (84.2 per cent) were treated by pulmonary resection alone.

Results and Follow-up Evaluation.—Inasmuch as the cases vary so greatly both in regard to indications and the degree and length of improvement, it has proved impossible to classify them and present them in the form of a concise chart (Table V). Three cases have already been reported in detail.

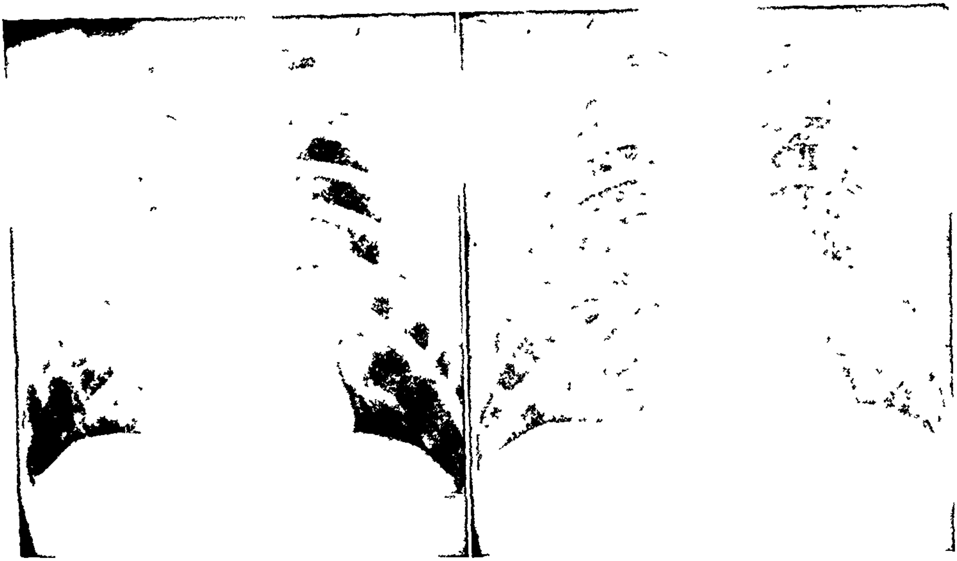

Fig 9 —Case 4 Pre- and postoperative x-ray studies of a 51-year-old white male high *school* teacher At thoracotomy a large emphysematous portion of the lung was found to be filling almost the entire left pleural space This emphysematous lung arose only from the superior segment of the lower lobe and was compressing the remaining lung tissue It was removed in wedge fashion

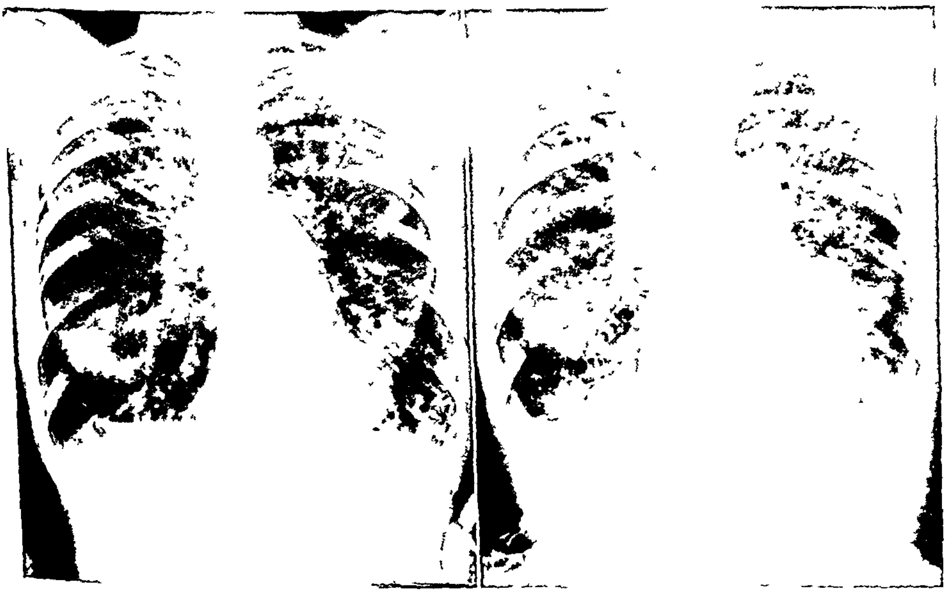

Fig 10 —Case 5 Pre- and postoperative x ray studies of a 51-year-old white woman Symptoms had been those of progressive dyspnea, cough, and sputum production for 10 to 12 years; more severe since an episode of pneumonia 2 to 3 months prior to admission The films show emphysema and a bleb-like area in the lower two-thirds of the right lung field Bronchograms revealed universal bronchiectasis At thoracotomy, with the patient maintained *on a* mechanical respirator, a markedly emphysematous middle lobe was resected Thereafter, she was markedly improved, but has shown signs of early cor pulmonale 18 months after the operation

Table V. Results in 19 Patients Operated Upon for Localized Vesicular or Bullous Emphysema

CASE NO.	AGE	RACE	SEX	DATE OF SURGERY	POSTOP. DEATH	IMMEDIATE RESULTS			LATE RESULT: DATE SYMPTOMS RETURNED, DATE OF DEATH, AND PRESENT STATUS
						E	G	P	
367716	62	W	M	9/12/53	3			X	Operative death, Pseudomonas pneumonia
466035	65	W	M	1/11/58	26			X	Operative death, sudden death at home
474563	36	W	M	5/10/58	22			X	Operative death, pulmonary thrombosis
500669	57	W	F	7/9/59	3			X	Operative death, right heart failure
309197	22	W	M	3/15/50		X			Asymptomatic April, 1960: 10 yr. postop.
484538	51	W	M	10/23/58		X			Asymptomatic April, 1960; 8 yr. postop.
468852	68	W	M	2/16/58			X		Symptom return 3 mo. postop.: died 4 mo. postop.
423273	52	W	M	10/4/57		X			Symptom return 3 yr. postop.; died 3 yr. postop.
516345	56	W	M	2/22/60			X		Remains improved 3 mo. postop.
510871	58	W	M	2/8/60			X		Remains improved 3 mo. postop.
507580	64	N	F	11/6/59			X		Remains improved 6 mo. postop.
11789	56	W	M	4/9/59			X		Symptom return 4 mo. postop.; now progressive
511734	58	W	M	2/23/59		X			Symptom return 6 mo. postop.; now progressive
412890	46	W	M	7/27/55			X		Symptom return 7 mo. postop.; now progressive
508893	49	W	M	5/18/59			X		Still some dyspnea 1 yr. postop.
484503	51	W	F	11/25/58		X			Cor pulmonale 1 yr. postop.
442967	45	W	F	4/21/54			X		Symptom return 2 yr. postop.; now progressive
508608	54	W	M	9/10/52		X			Symptom return 3 yr. postop.; now progressive
427042	55	W	F	5/17/56		X			Still working 4 yr. postop.: mild symptoms

One of these patients whose emphysema was limited to one segment and another one with a tremendously emphysematous accessory lobe appear to be permanently cured. Two patients have died of progressive disease 5 months and 3 years, respectively, since operation. Three patients have been followed for a maximum of 6 months, and remain much improved at the present time. The remaining 8 patients have had a return of symptoms from 4 months to 4 years after operation. Of these, only 1 does not show signs of progressive deterioration and she is actively employed 4 years after pulmonary resection.

Here again, as in the patients operated upon for emphysematous blebs complicated by generalized emphysema, although the immediate result may be excellent, the patients usually have a return of their symptoms which become progressive and eventually cause their death.

SUMMARY AND CONCLUSIONS

Fifty cases of emphysematous blebs and localized vesicular and bullous emphysema treated by Monaldi intracavitary suction or open surgical resection are reported.

The cases are divided into two groups. The first includes cases of emphysematous blebs complicated or uncomplicated by generalized emphysema. The second includes all cases of localized vesicular and bullous emphysema. At the present time, although it may be advisable, we have not operated upon patients with generalized disease alone, feeling that in such cases there is too little normal lung present.

The surgical indications for each group are defined and illustrative cases are presented. The open operation has become the preferred surgical approach in most instances. The operative mortality for the entire group was 8 per cent.

The immediate and late results are tabulated. In those cases of emphysematous blebs uncomplicated by generalized emphysema, the immediate effect is excellent and permanent. In spite of an excellent early result, patients with blebs complicated by generalized emphysema and those with localized vesicular and bullous emphysema note a return of their symptoms at varying periods of time. These symptoms then become progressive and the majority of cases terminate in right heart failure. However, these discouraging results in such patients should not deter us from operating upon them, for they are markedly benefited over a significant period of time by resection of the most severely involved areas.

REFERENCES

1. Clagett, O. T.: Surgical Treatment of Emphysematous Blebs and Bullae, Dis. Chest 15: 699, 1949.
2. Weisel, W., and Slotnik, I.: Emphysematous Bulla Complicated by Hemorrhage and Infection, Treated With Surgical Drainage, Am. Rev. Tuberc. 61: 742-746, 1950.
3. Welchous, G. A., and Massie, J. R., Jr.: Pulmonary Blebs and Bullae, South. Surgeon 16: 768-776, 1950.
4. Dugan, D. J., and Samson, P. C.: Surgical Treatment of Emphysematous Blebs and Pulmonary Tension Cysts, J. THORACIC SURG. 20: 729-748, 1950.
5. Crenshaw, G. L., and Fowler, D. F.: Surgical Management of Pulmonary Emphysema, J. THORACIC SURG. 24: 398-410, 1952.
6. Cooke, F. N., and Schaff, B.: Surgical Management of Emphysematous Blebs and Bullae, South. M. J. 46: 474-480, 1953.
7. Massie, J. R., Jr., and Welchous, G. A.: Pulmonary Blebs and Bullae, Ann. Surg. 139: 624-634, 1954.
8. Salzberg, A. M., and Blades, B.: Surgical Management of Emphysematous Blebs and Bullae, J. Am. Geriatric Soc. 3: 15-20, 1955.
9. Jewsbury, P.: Surgical Therapy of Cystic Disease and Emphysema in Young Children, Brit. J. Surg. 42: 601-607, 1955.
10. Weisel, W.: Surgical Treatment of Localized Emphysematous Disease, Ann. Surg. 142: 17-27, 1955.
11. Walkey, H. E., and Wolcott, M. W.: Surgical Treatment of Bullous Emphysema, Dis. Chest 28: 638-650, 1955.
12. Symposium: Surgical Treatment of Emphysematous Bullae, Am. Rev. Tuberc. 74: 856-873, 1956.
13. Siebens, A. A., Grant, A. R., Kent, D. C., Klopstock, R., and Cincotti, J. J.: Pulmonary Cystic Disease; Physiologic Studies and Results of Resection, J. THORACIC SURG. 33: 185-212, 1957.
14. Capel, L. H., and Belcher, J. R.: Surgical Therapy of Large Air Cysts of the Lung, Lancet 272: 759-762, 1957.
15. Blades, B., and Gwathmey, O.: Surgical Treatment of Emphysematous Blebs, M. Ann. District of Columbia 26: 119-124, 1957.
16. Fitzpatrick, M. J., Kittle, C. F., Lin, T. K., and Dowell, J. C.: Some Physiologic Changes Associated With Surgical Excision of Emphysematous Bullae, Am. J. Med. 22: 534-548, 1957.

17. DeBord, R. A.: Surgical Treatment of Pulmonary Cysts and Spontaneous Pneumothorax, Illinois M. J., 112: 163-164, 1957.
18. Sanderud, A.: Surgery of Localized Emphysema, Acta chir. scandinav. 117: 1-7, 1959
19. Sato, R., Yoshida, S. and Uchida, H.: Pre and Postoperative Cardiopulmonary Dynamics of the Emphysematous Bulla, J. THORACIC SURG. 39: 516-530, 1960
20. Head, J. R.: Pulmonary Cysts and Emphysematous Blebs and Bullae in Roentgenology of the Chest, Springfield, 1958, Charles C Thomas, publisher.
21. Head, J. R.: Cystic Disease of the Lung With Emphasis on Emphysematous Blebs and Bullae, Am. J. Surg. 89: 1019-1022, 1955.
22. Laennec, R. T. H.: Treatise on Diseases of the Chest and Mediate Auscultation, 1819
23. Head, J. R.: Observations of the Mechanism of Emphysema and the Surgical Treatment of Dyspnea, Quart. Bull. Northwestern Univ. M. School 25: 210-216, 1951
24. Head, J. R., and Avery, E. E.: Intracavitary Suction (Monaldi) in the Treatment of Emphysematous Bullae and Blebs, J. THORACIC SURG. 18: 761-776, 1949.
25. Korol, E.: Correlation of Carcinoma and Congenital Cystic Emphysema, 10 Cases, Dis Chest 23: 403-411, 1953.
26. Peabody, J. W., Jr., Katz, S., and Davis, E. W.: Bronchial Carcinoma Arising in a Lung Cyst, Am. J. Roentgenol 77: 1048-1050, 1957.
27. West, J. P., and Van Schoonhoven, P. V: Carcinoma of the Lung Developing in a Congenital Cyst, Surgery 42: 1071-1076, 1957.
28. Rothstein, E.: Infected Emphysematous Bullae, 5 Cases, Am. Rev. Tuberc. 69: 287-296, 1954.
29. Brantigan, O. C.: Surgical Treatment of Pulmonary Emphysema, Maryland State M. J. 6: 409-414, 1957.
30. Brantigan, O. C., and Mueller, E.: Surgical Treatment of Pulmonary Emphysema, Am. Surgeon 23: 789-804, 1957.
31. Brantigan, O. C., Mueller, E., and Kress, M. B.: A Surgical Approach to Pulmonary Emphysema, Am. Rev. Resp. Dis. 80: 194-206, 1959.

Discussion

DR. JOSEPH GORDON, Albuquerque, N. Mex.—I should like to tell you about our very limited experience in a small group of cases in New Mexico at the Veterans Administration Hospital.

This problem has been very well presented in the previous paper, and it is a difficult one in which we are still trying to find our way The group of patients which we have studied were operated upon by Dr. Wesley Childs, who was then Chief of Service and is now associated with Dr. Charles Bailey.

The patients were all severely distressed. They had a maximum breathing capacity of under 30 per cent, and these were patients who were unable to get around. Since they were veterans they were hospitalized and remained almost incapacitated in their present condition

This problem does not lead us to find our way directly, because of the admixture of such things as diffuse emphysema, solitary cyst, and bullae that may occur in one individual I have chosen the slides of one particular case to show you what our experience has been in this instance, from which some help has been drawn.

(Slide) The x ray film which you see is not unlike some of those which were shown previously. On the right side there is a giant sized space occupying emphysematous bulla or bleb, as we may choose to term it. This is a matter of definition. On the other side in the left lower third of the chest, there are multiple cystlike changes in contrast to the right side.

Following this, bronchograms were done which you will see in the next slide. (Slide) On the right you see the evidence of the space occupying bullous emphysema with constriction of the bronchial tree. On the left side there is evidence of a relative paucity of bronchial arborization.

The patient was operated upon on both sides. On the right side, an upper lobectomy was done. Prior to this the patient had a maximum saturation of 84 per cent oxygen in his blood; after this he had a 92 per cent oxygen saturation On exercise the unusual observation was made that it became 94 per cent, indicating that there had been improvement in circulation.

Some time later the left lung was operated upon by oversewing of the emphysematous blebs rather than by excision However, after this second operation the patient showed some deterioration, and I should like to show you in the next slide what we have noted in the bronchogram

(Slide) There is good reorientation of the bronchogram on the side on which operation was followed by good results, and there is poor reorientation on the left side, on which operation was followed by further deterioration in the patient It is to be concluded that the reorientation of the bronchial tree to a more nearly normal pattern was followed by marked functional improvement The poorer bronchogram seen on the second or the left side following operation was accompanied by deterioration in functional capacity.

DR W EMORY BURNETT, Philadelphia, Pa —It is a great opportunity on this occasion to hear about these remarkable experiences with this miserable and progressive disease

Since the senior author suggested two stage drainage several years ago, we have all used it now and then because it has a very useful purpose It permits improvement with very little surgery in some of these poor risk patients and permits of multiple attack which is also a great advantage It has been a very helpful method

(Slide) The combinations mentioned today have been extremely useful in our hands as well as theirs; (slide) namely, on this upper lobe situation They have prolonged patients' lives indefinitely, although ordinarily it is a progressive disease with a miserable outcome

In some, as you see here (slide), there is a fairly localized disease with a large bulla on one side and a fairly good lung on the other. It certainly seems wise to operate and remove the diseased area Some of these patients have received tremendous benefit

(Slide) This same patient, 5 years later, shows some further progression but has had a greatly improved function in the interim and even at this time

When the disease is bilateral, but more marked on one side than the other, one also finds it worth while to operate Occasionally, one is surprised to find that the disease is almost completely confined to one lobe which can be removed In these situations one can produce excellent temporary benefit

(Slide) Finally, I'd like to call attention to the fact that a marked degree of obstructive emphysema may accompany carcinoma which may be overlooked Such a condition is readily demonstrated by inspiration expiration films and one should be on the watch for such a lesion

(Slide) Last, I'd like to call attention to the fact that a marked degree of destructive emphysema may accompany carcinoma which may be overlooked

DR OTTO C BRANTIGAN, Baltimore, Md—I would like to call attention to two points· First, there is a disturbance in vascularity. The slide shows an emphysematous lung with the pulmonary artery injected It shows the disturbance to be primarily in the capillaries of the alveoli Second, in primary hypertrophic obstructive bilateral pulmonary emphysema, there is obstruction to the outflow of air from the lung There is no known etiology and there is controversy about the initial cause of airway obstruction, but in the later stages of the disease there is obviously an interruption of the physiologic mechanism that holds open the bronchioles The physiologic principle involved in holding open the collapsible bronchioles depends upon an elastic lung which is held expanded by a rigid chest wall and a closed pleural space The elasticity of the lung causes a negative intrapleural pressure and a circumferential force that holds open the bronchioles Normally, on inspiration, bronchi and bronchioles enlarge in diameter, on expiration, they decrease in diameter When primary emphysema, with or without blebs, or bullae, is fully developed, the loss of this physiologic principle is an important factor in expiratory airway obstruction, regardless of its etiology or initial cause In primary hypertrophic obstructive bilateral pulmonary emphysema, with or without blebs, or bullae, the expiratory volume of the lung is much larger than normal Pulmonary emphysema is similar to stuffing 6,000 or 7,000 c c of lung into a pleural space of 5,000 c c volume. In such a situation, the circumferential pull holding open the bronchioles is lost to a greater or lesser degree

It would seem that in any surgical attack upon the disease, one must return this lost physiologic mechanism and it can be done in some degree by reducing the lung volume.

Dr. Head indicated that their patients, by the progression of disease after operation, lost the benefit gained by surgery. I would like to call attention to the fact that pulmonary emphysema is a bilateral disease. If both sides are not operated upon, there will be progression of disease in the unoperated lung. I suspect their patients will show progression of disease in the unoperated lung when the benefit gained by the first operation is lost. In the patients whom I have operated upon, there has been no progression of disease in the lung operated upon. At the present time there has been no loss of benefit gained by operation in the patients that have had bilateral operations. The longest follow-up is 8 years. In time, there must be some loss of benefit gained by surgery since emphysema is a disease of aging.

DR. OSLER ABBOTT, Atlanta, Ga.—Our group has had a major interest in this problem for some 15 years. We cannot concur in "the horrible long-term outlook" expressed by Dr. Head and his co-workers. Certain patients have had purely isolated bullous disease associated with normal lung. In this group, adequate excision has not been followed by the appearance of any progressive pulmonary degenerative process. In the other group in which bullous emphysema and the so-called hypertrophic obstructive type of emphysema is combined, we have not seen "progressive deterioration." Fundamentally, the problem is that surgical excision of bullae compressing adjacent areas of hypertrophic obstructive emphysema is only a part of the total treatment of this latter disease. In many instances, appropriate concomitant pulmonary denervation should be done. In all instances, a continuous, assiduous, and vigorous over-all nonsurgical treatment regimen must be instituted and continually monitored. Such a regimen must include (a) total abstinence from tobacco, (b) separation from other known sources of bronchial irritation, (c) control of associated bronchial infection and allergies, (d) refunctionalizing intercostal and diaphragmatic exercises, (e) bronchodilators, (f) expectorants, and (g) other supportive measures as indicated. To expect surgical procedures alone to stem the progress of pulmonary emphysema would appear to be a misunderstanding of one of the basic principles in the management of any type of chronic disease due to a combination of multiple causative factors.

At the present time, we have embarked on a prolonged study of emphysema therapy. We start with an extensive objective evaluation program including (a) roentgenograms, cinefluoroscopy, and pulmonary angiography, (b) cardiac catheterization, and (c) complete pulmonary function tests. At yearly intervals these tests are repeated. Four protocols of treatment used include: (1) steroids, chemotherapy, chest exercises, and bronchodilators, (2) the same combination as No. 1 plus multiple bronchoscopy, (3) multiple bronchoscopy, expectorants, chest exercises, bronchodilators—but no steroids, and (4) the same regimen as No. 3 plus surgical excision of localized advanced areas of disease plus pulmonary plexectomy.

The principle on which we base surgical therapy is that "when the finer pulmonary vasculature persists in patients with hypertrophic obstructive emphysema, there also is found persistence of the other components of the lung essential for useful respiratory function." A corollary to this principle is that "pulmonary emphysema is initially a disease of single or multiple major foci and the reflection of this primary localization persists even in terminal cases."

In view of this attitude we now place an increasingly major interest in pulmonary angiography. If such studies show compression of areas of the lung containing finer vascular components, then removal of an avascular area of lung distended by diffuse obstructive emphysema will release a potentially useful area. At surgery the effect of blockade of the pulmonary autonomic nervous system is studied. We study initially the effect of such blockade upon the per stroke volume of air delivered by "pressure constant, volume variable" ventilation assistor. Second, we are interested in the effect upon the gradient between the pulmonary artery and the venous pressure. Third, we study the effect upon the mean pulse pressure of the pulmonary artery and venous tracings. If sufficient beneficial functional response is noted in these studies, we add a pulmonary plexectomy to the selective excision of distended nonfunctioning lung tissue. In our experience, the postoperative course of these patients is often difficult, but controllable. Mortality rate is within reasonable limits. Long-term benefits have been obtainable, but attention to continued intensive prophylactic, rehabilitative, and therapeutic measures is mandatory.

DR. RICHARD H. OVERHOLT, Boston, Mass.—Dr. Head and his associates have clearly pointed out the manner by which structural defects alter the movement of air, its occupancy within, and availability of diffusing surfaces. The value of pre- and postoperative respiratory assistance has been stressed, if borderline cases are to be accepted for surgery.

Now, regardless of the extent of the structural changes, many patients have their functional capacities further reduced by an irritated air tube system. Mucosal swelling causes narrowing, and excessive secretions occlude or spill over to cause spasms of other bronchi. Countless check valve mechanisms then operate at the bronchiolar level. These are the net effects of a chemical bronchitis induced by the inhalation of tobacco smoke.

They are reversible. A period of 2 to 6 weeks usually results in substantial improvement. Many cases which we previously rejected on grounds of functional inadequacy now are being accepted. Even in good risk patients the convalescence is smoother if there is a period of freedom from chemical irritation in advance of the intervention. Many of the patients with poor pulmonary function learn this and have already stopped smoking before we see them.

Now, Dr. Head's experience and that of others' with generalized emphysema bear out that it is very difficult to correct it by surgical means. Fortunately, this disabling pulmonary disease can be prevented. Dr. Lowell and others have called attention to the fact that simple diffuse emphysema is usually an acquired disease. In the great majority of cases it represents a lung worn out by years and years of filtering out tobacco tars. Surgeons can relieve more suffering and prolong the lives of more people by advice on the prevention of emphysema than they can by the skillful application of the scalpel.

DR. WILLIAM M. TUTTLE, Detroit, Mich.—I just want to say one thing which I think has been missed in much of this discussion, and that is that emphysema is, after all, a result of aging, and aging can come differently to different people. Some people age much younger than other individuals. As you lose the elasticity of your alveoli, you also are probably losing it in your face. You become more wrinkled and you become more tired-looking, like I do. [Laughter]

However, I do agree with the authors that the removal of individual large blebs or emphysematous cysts, whichever you want to call them, is a fortunate thing, and I think it works. I think to operate bilaterally on emphysematous individuals is a perfectly foolhardy situation, and I do not think any surgeon should do it. I feel that you must consider emphysema, and realize that some of these individuals must be told that they will have to live with their emphysema, which they are going to have to do. Furthermore, there is no question in my mind that until tobacco has been proved to be a cause we should leave the matter out.

Now, I was once on a program with Dr. Overholt in which he criticized me for smoking, and I told him that my mother had once told me, "If you are not afraid of anything, you will never catch it," and I never did. [Laughter and applause]

PRESIDENT ADAMS: Many of you don't appreciate that the discussions at the present time are far different than what they were 20 years ago. Dr. Tuttle is injecting into this discussion something of the controversy and the argument that we used to see very often.

DR. HUDSON (Closing).—I think there probably will be no exception taken to the statement that blebs, bullae, that occupy much space or that cause much shortness of breath or that can be shown to be increasing with serial x rays, should be resected. When these situations are complemented by what I like to call chronic obstructive pulmonary emphysema, the situation becomes entirely different, and this is where the argument begins.

It is my feeling that people with chronic obstructive pulmonary emphysema should be operated on only after a thorough, thoughtful consideration of each case, both from a physiologic standpoint and also from a socioeconomic standpoint. This is very important not only to the individual but to his family group.

As surgeons, we rarely see chronic obstructive pulmonary emphysema except when it's got to its final or surgical point. I agree with Dr. Overholt and Dr. Abbott, and the others that have mentioned it, that there is a point in chronic obstructive pulmonary emphysema where it is reversible. I don't know just where this point is, but I base this experience on several patients who have studies indicating severe pulmonary emphysema without discernible changes in the lungs on the roentgenogram.

By taking these patients off cigarettes and by giving them the various things that the medical men give them for this disease, they have become rehabilitated and have continued to lead good lives without shortness of breath.

I would like to thank all the discussers for their interest, and I believe we too have learned something from them.

LUNG ABSCESS IN JAPAN

Kingo Shinoi, M.D. (by invitation), Tokyo. Japan*

Since 1935. I have had the opportunity to observe nearly 2,000 patients under treatment for various types of lung disease: composed of 1.200 cases of tuberculosis. 551 cases of lung abscess. 210 cases of lung cancer. 105 cases of bronchiectasis, and 30 cases of miscellaneous conditions. In these patients I have made special studies of lung abscess, which I wish to present on this occasion.

I. ETIOLOGY OF LUNG ABSCESS SEEN IN JAPAN

Analysis of 19.916 autopsy records. collected from the principal medical colleges in Japan. reveals that lung abscess was present in 638 cases. The putrid type of lung abscess was seen in 44 per cent of these—the non-putrid type in 56 per cent. However, the data in my clinic indicate that the putrid type has been found in 95 per cent of all cases. since the majority of patients suffering from the non-putrid type of the disease. which is hematogenous in origin. either die with their disease undiagnosed or recover by chemotherapy (Table I).

TABLE I. LUNG ABSCESS IN JAPAN

	AUTOPSY CASES	CLINICAL CASES
Putrid	282 (44%)	523 (95%)
Non putrid	356 (56%)	28 (5%)

In 1938, I demonstrated experimentally that this disease was produced mainly by bronchoembolism. but 53 per cent of the patients treated in my clinic had developed the disease by aspiration of undetermined nature as shown in the Table II. and 76 per cent of these showed evidence of dental disease. The postoperative incidence was only 5.1 per cent. much lower than in Europe and America. This may be attributed to the relatively infrequent use of general anesthesia. which is practically never used in oral surgery.

II. PATHOLOGIC STUDIES

Lung abscess. especially in the chronic stage. is essentially a state of pyofibrosis in which abnormal proliferation of bronchial mucous epithelium occurs.

Read at the Fortieth Annual Meeting of The American Association for Thoracic Surgery at Miami Beach, Fla., May 11-13, 1960.

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TABLE II. ETIOLOGY OF LUNG ABSCESS IN JAPAN

Aspiration of unknown cause	53.0%
Foreign body	5.1%
Postoperative	5.1%
Vomiting due to gastrointestinal and brain diseases	5.1%
Diseases of oral cavity, nose, and pharynx	2.1%
Bronchiectasis	12.4%
Tuberculosis	5.5%
Bronchial tumor	15.0%
Injury	0.4%
Perforation of esophageal carcinoma	0.4%

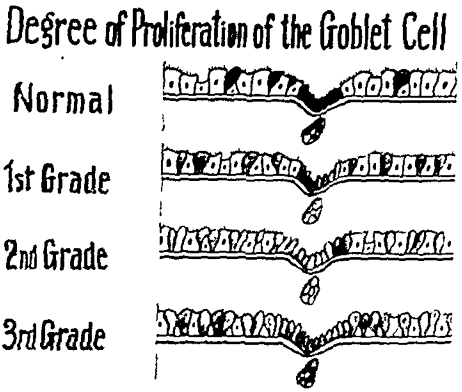

Fig. 1.—Degree of proliferation of the goblet cell. (Goblet cell is indicated as black cell.)

Such proliferative processes may involve columnar proliferation, squamous metaplasia, atypical proliferation, adenomatous metaplasia, and hyperplasia of goblet cells, all of which, excepting the proliferation of goblet cells, must be regarded as constituting carcinogenic matrices. Proliferation of columnar epithelium is chiefly encountered in large and medium bronchi, as shown in Table III, squamous cell metaplasia and atypical proliferation in the cavity wall, and adenomatous metaplasia in the bronchioles.

TABLE III. PROLIFERATION OF EPITHELIUM AND ITS SITE OF ORIGIN IN BRONCHUS

	LARGE	MEDIUM	CAPILLARY	CAVITY WALL
Columnar	84.3%	88.5%	3.8%	13.5%
Squamous	2.3%	23.1%	0	83.8%
Atypical	0	0	0	0
Adenomatous	0	0	53.8%	0
Cancerous			1.3%	

Careful search was made for carcinoma in situ and only one instance of minute carcinoma was found in 71 cases. This was detected in the region presenting adenomatous metaplasia of a chronic inflammatory lesion, accompanied by bronchiectasis in the left lower lobe, and was only as large as a millet grain. Although the incidence is only 1 per cent, there is a possibility of such a focus furnishing a carcinogenic matrix.

The significance of goblet cell proliferation in the production of sputum requires comment. These cells are normally present in relatively large numbers around the orifices of the mucous gland but, in this location, they are found in the proportion of one to ten of ciliated epithelial cells, as shown in Fig. 1. In pyofibrous lesions, however, the goblet cells are greatly proliferated, the degree of hyperplasia being designated as first grade in which the proliferative ratio of ciliated epithelium to goblet cells is 5:1, the second grade with the ratio of 3:1, in which the goblet cells show swelling, and the third grade with predominance of the mucus-filled goblet cells, some even suggesting the mucous membrane of gastrointestinal tract, as illustrated in Fig. 1. In lung abscess and bronchiectasis the proliferative changes are mostly of the second and third grades, being much more marked in other diseases, as shown in Table IV.

TABLE IV. DEGREE OF PROLIFERATION OF THE GOBLET CELL IN VARIOUS LUNG DISEASES

	ABSCESS	BRONCHIECTASIS	TUBERCULOSIS	CANCER
Normal	15.4%	10.0%	63.3%	66.7%
1st Grade	40.5%	20.0%	26.7%	33.3%
2nd Grade	30.8%	30.5%	10.0%	0
3rd Grade	13.4%	35.0%	0	0

As to relation of the proliferation of goblet cells to sputum production, it is evident that quantities of sputum exceeding 100 c.c. are associated with the second and third grade proliferation, whereas those of 50 c.c. or less are associated with either the first grade or normal, as shown in Table V. The sputum expectorated during the chronic stage contains more mucus with a higher pH but lower viscosity and specific gravity because of a lower protein content, when compared with that of the acute stage. These findings indicate that the goblet cells are intimately concerned with the production of sputum rich in mucus during the chronic stage.

TABLE V. RELATION BETWEEN SPUTUM VOLUME AND PROLIFERATION OF THE GOBLET CELL

	0-10 c.c.	10 c.c.-50 c.c.	50 c.c.-100 c.c.	100 c.c.-200 c.c.
Normal	40.0%	5.8%	0	12.5%
1st Grade	46.6%	52.9%	16.6%	23.0%
2nd Grade	13.4%	35.2%	50.0%	35.0%
3rd Grade	0	5.8%	33.0%	27.0%

III. SOME CLINICAL PROBLEMS

Of 551 cases of lung abscess treated in our clinic, 338 patients belonged to the preantibiotic age and the remainder to the postantibiotic age; the two groups show definite differences in many ways. The incidence of silent abscess or recurrent abscess is high in the former group, presenting variable clinical pictures. On the other hand, complications, such as cerebral abscess or empyema, are apparently decreased. Bacteria found in the sputum are usually fuso-spirochetal in type during the acute stage, often changing to drug-resistant staphylococcal type, probably the result of long-continued ineffective chemotherapy.

Operative intervention is indicated in patients with chronic disease who have had chemotherapy up to 1 month. It is important to bear in mind in proceeding with the operation that the chronic cases are wet cases complicated by lowered cardiopulmonary function.

Thus, in chronic recurrent cases of lung abscess, the alveolar function is reduced when fibrosis of the lesion occurs extensively, and, in cases characterized by abundant sputum, the disturbance of ventilation leads to latent anoxia and produces an additional load on the right heart.

In determining the indication for lung resection, the functional limits should be set at 40 per cent or over of vital capacity, 61 per cent or less of residual air, 82 per cent or more of ventilatory reserve ratio, 85 per cent or over of arterial oxygen saturation, and 20 mm. Hg or less of pulmonary arterial pressure, as shown in Table VI. These requirements are therefore far more strict than in lung resection for tuberculosis.

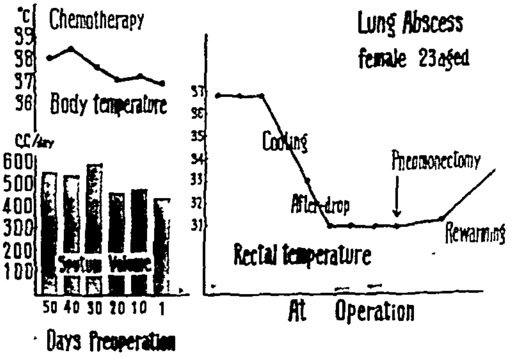

Fig. 2.—Quantities of bronchial secretion before and after operation under hypothermia.

TABLE VI. INDICATION FOR OPERATION OF WET CASE

Per cent of predicted vital capacity		more than 40 %
Residual volume/total lung capacity	100	less than 60%
Ventilatory reserve ratio		more than 82%
Sao_2		more than 85%
Pulmonary arterial pressure		less than 20 mm. Hg

The pulmonary capacity is reduced upon cessation of sputum production after lung resection, but both ventilatory and alveolar function are markedly improved, although no immediate amelioration of the circulatory burden occurs.

Disposal of secretion discharged during the operation on a wet case, such as a lung abscess, is an important problem for consideration. It is desirable to convert the disease into a dry case preoperatively by means of chemotherapy, bronchial lavage, and postural drainage, but if these measures are ineffective the application of artificial hypothermia is utilized. With the reduction of rectal temperature to 30° C. or lower by cooling the entire body, the secretion of the air passage ceases and operation can be performed in a dry state. Fig. 2 is a chart of a patient with a lung abscess of the entire right lung, who expectorated as much as 500 c.c. of sputum daily, in whom the respiratory tract becomes so free from secretion under general hypothermia that operation could be performed without difficulty.

Animal experiments show that bronchial secretion is decreased by reason that gastric secretion declines under hypothermia (Fig. 3). Bronchial ciliary movements are depressed (Fig. 4). Moreover, extracellular fluid of the lung is less in the state of hypothermia (Fig. 5).

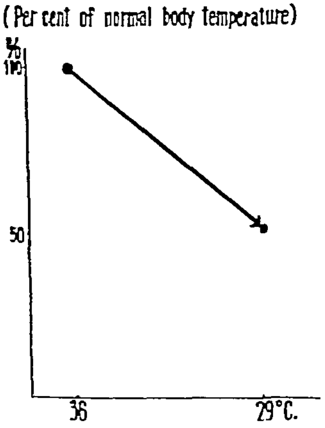

Fig. 3.

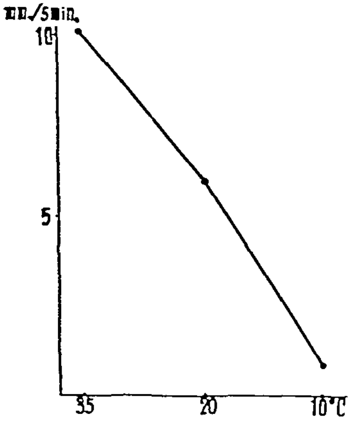

Fig. 4.

Fig. 3.—Influence on gastric secretion in hypothermia.
Fig. 4.—Bronchial ciliary movement (mm. per 5 min.) in hypothermia.

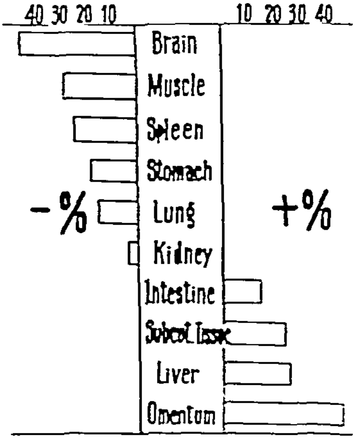

Fig. 5.—Change of extracellular fluid in hypothermia.

Table VII summarizes the therapeutic results which indicate that, before the advent of antibiotics, 13 per cent of patients responded to chemotherapy, 35 per cent to intratracheal administration of iodized oil, and 54 per cent were cured by pneumonotomy, with a mortality rate of 40 per cent.

TABLE VII. RESULTS OF TREATMENT

METHOD OF TREATMENT		CURE RATE	MORTALITY RATE
Preantibiotic			
Chemotherapy	86	13%	34%
Iodized oil	155	35%	
Pneumonotomy	131	54%	40%
Postantibiotic			
Chemotherapy	81	65%	4%
Pneumonotomy	27	60%	20%
Lung resection	100	96%	4%

However, 65 per cent of patients treated with antibiotics showed satisfactory improvement, and pneumonotomy produced cure in 60 per cent. Most of the patients were subjected to lung resection with a cure rate of 96 per cent.

The incidence of postoperative empyema is 23 per cent, a complication commonly encountered in cases of drug-resistant lung abscess. It may be stated in conclusion that most of the patients operated upon in Japan belong to the drug-resistant group, but it is now possible to achieve complete cure of this disease by proper change from chemotherapy to surgery.

DISCUSSION

DR. W. EMORY BURNETT, Philadelphia, Pa.—I want particularly to thank Dr. Shinoi for coming such a great distance to give us the benefit of his extensive experience with this dangerous disease.

In our own experience this had been for several years an almost unknown lesion at Temple University Hospital, until the last 3 or 4 years, during which time there has occurred a progressive increase in admissions for lung abscess. This may be due to the increase in resistant staphylococci, either alone or in combinations—more resistant than they were in the earlier group of lung abscesses, of which there were 115.

From my report some 20 years ago in the *Pennsylvania Medical Journal*, I wish to recall an extremely useful adjunct to treatment; namely, aspiration under fluoroscopy with instillation of high concentrations of antibiotics directly into the cavity. Such concentrations can never be reached by systemic administration and the insulation from the blood stream of this dead tissue makes the contrast even greater.

(Slide) This patient was admitted 10 days after he had been chilled in a cold rain while changing an auto tire, and one sees an obvious abscess which progressed to this marked degree in the period of the next 3 weeks (slide) on systemic antibiotics.

(Slide) The next slide presents the picture 5 days later. Starting on the date of the previous roentgenogram, the patient had two aspirations on consecutive days with the removal of some 50 c.c. of odorous pus the first time and the second time obtaining air only without pus. In each instance 500,000 units of penicillin was injected plus one gram of streptomycin on the second occasion. The temperature dropped to normal in 2 days, and expectoration was reduced almost completely. One can see the rapid improvement in these few days by roentgenograms also.

(Slide) Five months later he appears to be well clinically and by x-ray studies.

(Slide) We also noted that bronchograms of these patients, who were treated in this fashion early in their course, showed no residual bronchiectasis as seen in this instance. (Slide) On this slide of 9 patients successfully treated in this fashion, I would like you to notice how few aspirations were required for each patient—only two or three in most instances.

(Slide) There were 4 others in this series in which there was inadequate diagnosis, pneumothorax, or, in one instance, a slow response in which open-surgery had to be done.

Of the potential complications, pneumothorax occurred in 2 patients. One had apparently received adequate effect of previous aspirations and rapidly recovered. The other had not and required surgery, as listed in the 4 requiring surgery.

Hemoptysis did not occur, possibly because of the accuracy of guidance into the cavity by fluoroscopy. It should be insignificant if it did occur.

Empyema, although feared greatly in the early cases, was not encountered. Possibly this was because of the injection of antibiotic solution throughout the entire withdrawal of the needle to spill the last few drops on the skin, thus decontaminating at the same time that contamination occurred. Neither was air embolism observed. For details I would refer you to the article ''Pulmonary Suppuration'' (Pennsylvania M. J. 40: 1045-1051, 1937).

(Slide) Chronic abscess, of course, has to be resected without question, but one can clean it up considerably by the same method and produce a state of better nutrition for the patient and less chance of postoperative infection.

If you are unfortunate enough to see an occasional abscess again, I should like to highly commend to you this simple and promptly effective method.

PROFESSOR SHINOI (Closing).—Thank you very much for the discussion.

However, I cannot answer in detail because my English is poor, but I wish to make additional studies of this problem.

A STUDY OF ESSENTIAL HEMOPTYSIS

Raymond J. Barrett, M.D., and William M. Tuttle, M.D., Detroit, Mich.

HEMOPTYSIS is correctly considered to be an ominous sign by physician and patient alike. In from 82 to 96 per cent of various reported series it has been found to be associated with serious underlying disease (Table I). The exact incidence of each lesion cannot be accurately determined since the structure of most reported series is somewhat specialized. However, carcinoma, bronchiectasis, and tuberculosis are the three most common underlying disease processes. Broncholithiasis, bronchial adenoma, foreign bodies, pneumonia, lung abscess, pulmonary infarction, and cardiovascular disease account for most of the remaining cases. Hemoptysis of undetermined origin, the subject of this discussion, varies from 3.8 to 18 per cent in reported series.

TABLE I. INCIDENCE AND ETIOLOGY OF HEMOPTYSIS

	PER CENT OF INCIDENCE					
LESIONS	HELLER (416)*	SOUDERS (105)	MOERSCH (200)	ABBOTT (497)	JACKSON (436)	LEVITT (683)
Bronchial carcinoma	2.4	2.8	29.5	21	20	12
Chronic bronchitis	15	14	9	2	17	—
Bronchiectasis	7	28.5	26.5	21	32	15
Tuberculosis	40	1.9	5.5	22	—	50
Pneumonitis	6	—	3	1	6	1
Lung abscess	1	—	5	—	11	6
Cardiovascular	2	4.7	—	1.4	—	7
Other	1.5	31.1	14	27.8	6	4
Unknown	15	18	7.5	3.8	8	5

*Number of cases.

With such a serious potential, hemoptysis warrants an adequate diagnostic work-up regardless of its extent and whether it has ceased. A negative roentgenogram of the chest in no way relieves the physician of the responsibility for a determined effort to determine the cause of the bleeding. Bronchoscopy and, if negative, bronchography, along with study of the aspirate for tubercle bacilli and malignant cells, constitute a minimum study. Equivocal hilar shadows may require fluoroscopy, laminography, and angiocardiography to settle the question of hilar vessel prominence versus disease process. If the vascular dynamics within the pulmonary tree are suspect as the cause of bleeding, cardiac catheterization may be indicated. There will arise certain instances wherein the

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From the Department of Surgery, College of Medicine, Wayne State University, Harper Hospital, and Detroit Memorial Hospital.

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physician is not convinced that the blood is actually originating from the tracheobronchial tree. In such circumstances, barium swallow, esophagoscopy, and study of the oro- and nasopharynx and sinuses would be in order.

When one has exhausted the diagnostic armamentarium to no avail, the case is variously labelled as idiopathic hemoptysis or hemoptysis of undetermined origin. Speculation as to the subsequent course of this group precipitated the present study.

STUDY

Ninety-seven patients with hemoptysis of undetermined origin were studied between Jan. 1, 1950, and April 15, 1959. The composition of this group by age and sex is shown in Table II. Only one Negro patient, a 50-year-old woman who has been lost to follow-up, was present in the series and this is considerably below the usual proportion in our practice its significance is questionable. The ratio of 67 males to 30 females is in agreement with that noted in most reports. It will be noted that the highest incidence in both males and females was in the decade 40 to 50 and that the age group 40-60 accounted for over one half the patients of both sexes.

TABLE II. COMPOSITION OF SERIES

	AGE GROUP						
	20-29	30-39	40-49	50-59	60-69	70-79	
Male	2	11	21	17	13	3	
Female	1	5	9	9	5	1	
Total	3	16	30	26	18	4	97

The present status of 81 of the 97 patients (83.5 per cent follow-up) was determined as of April, 1960, by means of personal contact, consultation with the referring physician, or by direct mail query. The composition of the group followed is shown in Table III.

TABLE III. FOLLOW-UP

	FOLLOW-UP (YEARS)					PER CENT FOLLOW-UP
	1-3	3-5	5-7	7-9	9-10	
Male						
No. of patients	22	15	16	7	7	
No. followed	21	12	13	6	5	85
Female						
No. of patients	7	5	11	6	1	
No. followed	7	4	7	5	1	80
Total number of patients	29	20	27	13	8	
Total % followed	96.5	80	74	84	75	83.5

It will be noted that 44 patients were followed for periods ranging from 1 to 5 years while 37 were followed for intervals ranging from 5 to 10 years. We attach particular significance to the 96.5 per cent follow-up in the first 3 years after study since one might reasonably expect that carcinoma or tuberculosis, if related to the hemoptysis, should become clinically apparent in this interval.

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Male						
No. of patients	22	15	16	7	7	
No. followed	21	12	13	6	5	85
Female						
No. of patients	7	5	11	6	1	
No. followed	7	4	7	5	1	80
Total number of patients	29	20	27	13	8	
Total % followed	96.5	80	74	84	75	83.5

It will be noted that 44 patients were followed for periods ranging from 1 to 5 years while 37 were followed for intervals ranging from 5 to 10 years. We attach particular significance to the 96.5 per cent follow-up in the first 3 years after study since one might reasonably expect that carcinoma or tuberculosis, if related to the hemoptysis, should become clinically apparent in this interval.

A STUDY OF ESSENTIAL HEMOPTYSIS

Raymond J. Barrett, M.D., and William M. Tuttle, M.D., Detroit, Mich.

HEMOPTYSIS is correctly considered to be an ominous sign by physician and patient alike. In from 82 to 96 per cent of various reported series it has been found to be associated with serious underlying disease (Table I). The exact incidence of each lesion cannot be accurately determined since the structure of most reported series is somewhat specialized. However, carcinoma, bronchiectasis, and tuberculosis are the three most common underlying disease processes. Broncholithiasis, bronchial adenoma, foreign bodies, pneumonia, lung abscess, pulmonary infarction, and cardiovascular disease account for most of the remaining cases. Hemoptysis of undetermined origin, the subject of this discussion, varies from 3.8 to 18 per cent in reported series.

TABLE I. INCIDENCE AND ETIOLOGY OF HEMOPTYSIS

LESIONS	PER CENT OF INCIDENCE					
	HELLER (416)*	SOUDERS (105)	MOERSCH (200)	ABBOTT (497)	JACKSON (436)	LEVITT (683)
Bronchial carcinoma	2.4	2.8	29.5	21	20	12
Chronic bronchitis	15	14	9	2	17	—
Bronchiectasis	7	28.5	26.5	21	32	15
Tuberculosis	40	1.9	5.5	22	—	50
Pneumonitis	6	—	3	1	6	1
Lung abscess	1	—	5	—	11	6
Cardiovascular	2	4.7	—	1.4	—	7
Other	1.5	31.1	14	27.8	6	4
Unknown	15	18	7.5	3.8	8	5

*Number of cases.

With such a serious potential, hemoptysis warrants an adequate diagnostic work-up regardless of its extent and whether it has ceased. A negative roentgenogram of the chest in no way relieves the physician of the responsibility for a determined effort to determine the cause of the bleeding. Bronchoscopy and, if negative, bronchography, along with study of the aspirate for tubercle bacilli and malignant cells, constitute a minimum study. Equivocal hilar shadows may require fluoroscopy, laminography, and angiocardiography to settle the question of hilar vessel prominence versus disease process. If the vascular dynamics within the pulmonary tree are suspect as the cause of bleeding, cardiac catheterization may be indicated. There will arise certain instances wherein the

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physician is not convinced that the blood is actually originating from the tracheobronchial tree. In such circumstances, barium swallow, esophagoscopy, and study of the oro- and nasopharynx and sinuses would be in order.

When one has exhausted the diagnostic armamentarium to no avail, the case is variously labelled as idiopathic hemoptysis or hemoptysis of undetermined origin. Speculation as to the subsequent course of this group precipitated the present study.

STUDY

Ninety-seven patients with hemoptysis of undetermined origin were studied between Jan. 1, 1950, and April 15, 1959. The composition of this group by age and sex is shown in Table II. Only one Negro patient, a 50-year-old woman who has been lost to follow-up, was present in the series and this is considerably below the usual proportion in our practice—its significance is questionable. The ratio of 67 males to 30 females is in agreement with that noted in most reports. It will be noted that the highest incidence in both males and females was in the decade 40 to 50 and that the age group 40-60 accounted for over one half the patients of both sexes.

TABLE II. COMPOSITION OF SERIES

	AGE GROUP						
	20-29	30-39	40-49	50-59	60-69	70-79	
Male	2	11	21	17	13	3	
Female	1	5	9	9	5	1	
Total	3	16	30	26	18	4	97

The present status of 81 of the 97 patients (83.5 per cent follow-up) was determined as of April, 1960, by means of personal contact, consultation with the referring physician, or by direct mail query. The composition of the group followed is shown in Table III.

TABLE III. FOLLOW-UP

	FOLLOW-UP (YEARS)					PER CENT FOLLOW-UP
	1-3	3-5	5-7	7-9	9-10	
Male						
No. of patients	22	15	16	7	7	
No. followed	21	12	13	6	5	85
Female						
No. of patients	7	5	11	6	1	
No. followed	7	4	7	5	1	80
Total number of patients	29	20	27	13	8	
Total % followed	96.5	80	74	84	75	83.5

It will be noted that 44 patients were followed for periods ranging from 1 to 5 years while 37 were followed for intervals ranging from 5 to 10 years. We attach particular significance to the 96.5 per cent follow-up in the first 3 years after study since one might reasonably expect that carcinoma or tuberculosis, if related to the hemoptysis, should become clinically apparent in this interval.

CLINICAL INVESTIGATION OF THE HEMOPTYSIS

In the initial examination all patients had a bronchoscopy, bronchogram, and culture of the bronchial aspirate for tubercle bacilli. Sixty-nine of the 97 patients had study of the bronchial aspirate for malignant cells and 65 of these were reported negative. Of the remainder, 2 patients with a questionable smear are alive and well 1½ and 6 years later. A 33-year-old male had a report of "malignant smear"—4 years and 7 months later he had resection of a squamous cell carcinoma of the lip but his chest remains normal 5 years after the original report. One questionably malignant smear was reported in 1951 on a 54-year-old male with severe hypertension. He has been lost to the series and his present status is unknown.

Three patients had repeat negative bronchoscopies on occurrence of subsequent hemoptysis. Two patients had angiocardiography and 1 of these also had cardiac catheterization. One other patient had catheterization on a subsequent admission for recurrent hemoptysis.

One 64-year-old male had left exploratory thoracotomy in 1953 because of an equivocal hilar shadow, the nature of which could not be determined by laminography and angiocardiography. The shadow proved to be vascular in origin. Over 6 years later, he is alive and well, without recurrence of hemoptysis.

INITIAL EXTENT AND SUBSEQUENT RECURRENCE OF HEMOPTYSIS

Twenty of the patients (20.6 per cent of the series) presented with streaking (Table IV), whereas 77 (79.4 per cent of the series) were classified as having gross hemoptysis (Table V) varying from ½ teaspoonful to such an extent that one man required multiple transfusions.

TABLE IV. STREAKING

	MALES		FEMALES	
No prior episodes	13			1
Prior episodes		5	1	
Subsequent episodes	3	1	0	0
Lost to follow-up	0	0	0	0
Totals	18		2	

TABLE V. GROSS BLEEDING

	MALES		FEMALES	
No prior episodes	31		15	
Prior episodes		18		13
Subsequent episodes	1	4	2	2
Lost to follow-up	6	4	4	2
Totals	49		28	

It has been suggested that if the hemoptysis is recurrent one must suspect serious underlying disease. Reference to Tables IV and V will reveal that 37 patients either had episodes of hemoptysis extending over a period longer than

6 months prior to examination or subsequently bled at intervals over a period longer than 6 months after examination. Of this latter group, within 3 years, 3 patients showed evidence of serious vascular disease as an explanation of the bleeding. These will be analyzed in detail.

CASE 1.—H. R., a 39-year-old woman, was first seen in March, 1955, with a complaint of intermittent gross hemoptysis over a period of 12 years. Initial examinations, including angiocardiography, were negative. Three years later, in March, 1958, she was readmitted to the hospital because of recurrent increasing bleeding. Two attempts at cardiac catheterization were incomplete because of reactions during the course of the procedure. It was the opinion of the cardiologist, however, that she probably warranted exploration of the mitral valve. This was performed in July, 1958, with no evidence of mitral stenosis. A lung biopsy was taken at the same time and the final diagnosis was primary pulmonary hypertension. She is alive but continues to have episodes of hemoptysis at the present time.

CASE 2.—H. B., a 57-year-old white woman, was first seen in May, 1955, with a history of several episodes of gross hemoptysis in the preceding 18 months. Examination, including esophagoscopy, was negative. During the following 3 years she continued to have isolated episodes of gross hemoptysis, developed obvious signs of congestive failure, and is alive but in a deteriorating condition at the present time.

CASE 3.—K. B., a 40-year-old white man, was first seen in June, 1951, with a history of recurrent gross hemoptysis of 1 year's duration. Initial investigation was negative. Two years later he was readmitted because of recurrent bleeding. Cardiac catheterization proved this to be on the basis of mitral stenosis but operation was refused. He is alive with a grossly enlarged heart and in rapidly deteriorating condition.

In addition, one female (Case 4) continued to bleed intermittently following study and died 15 months later.

CASE 4.—M. D., a 54-year-old white woman, was first seen in November, 1958, with a complaint of gross hemoptysis of several days' duration. Investigation revealed no abnormalities. In June, 1959, she had another episode of gross hemoptysis. Repeat roentgenograms showed no abnormalities and no change. She was readmitted in February, 1960, in shock and died a few days later of a dissecting thoracic aortic aneurysm. There was no hemoptysis during the terminal episode and autopsy revealed no anatomic cause for the previous hemoptyses. Available evidence would indicate that they were isolated and unrelated phenomena.

In addition to the death reported above, 3 other patients are known to be dead—all of causes unrelated to the hemoptysis.

CASE 5.—A 63-year-old white man died 3 years after study from hemorrhage from the renal pedicle after a nephrectomy.

CASE 6.—A 58-year-old white man died 5½ years later from the last of three myocardial infarctions which had occurred in the succeeding years.

CASE 7.—A 52-year-old white man died, 21 months after study, from cirrhosis of the liver.

Patients still alive but with serious disease which has no apparent relation to the hemoptysis include: (a) a 33-year-old man, previously mentioned, who developed squamous cell carcinoma of the lip 4 years later; (b) a 42-year-old man who developed myocardial infarction 14 months later; (c) a 46-year-old woman who became psychotic 5 years later; (d) a 61-year-old man, a hypertensive, who developed a stroke 6 months later and a myocardial infarction

12 months later; (e) a 60-year-old man who developed carcinoma of the soft palate 18 months later; and (f) a 52-year-old man who has had two myocardial infarctions in the 9 years subsequent to study.

ANALYSIS OF THE VARIOUS THEORIES OFFERED TO EXPLAIN HEMOPTYSIS OF UNDETERMINED ORIGIN

1. *Mucosal Ulceration Beyond the Vision of the Bronchoscopist.*—

2. *Undetected Bronchiectasis of a Single Radicle.*—

We feel that it is impossible to either prove or disprove either of the above as the cause of the hemoptysis.

3. *Pulmonary Hypertension.*—Three patients in this group ultimately had their hemoptysis explained on this basis.

4. *Systemic Hypertension.*—Nine patients of the original 97 had systemic hypertension. One 54-year-old man has been lost to the series. The remaining 8 are alive and have not subsequently bled over intervals ranging from 18 months to 8 years.

5. *Blood Dyscrasias.*—There were no blood dyscrasias in this series.

6. *Small Infarct Without X-ray Evidence.*—This is impossible to prove or disprove. However, it strains the imagination to conceive that the many patients in this series who had multiple episodes of hemoptysis would never show x-ray evidence.

7. *Vicarious Menstruation.*—We are convinced of the existence of this syndrome and have seen it occur in other patients with a pulmonary lesion. There were no cases in this series, however, which met the criteria.

8. *Varicosities About the Carina and Upper Lobe Orifices.*—Smidt has ventured the opinion that a probable site of predilection for hemoptysis exists around the carina and upper lobe orifices. He feels that, even in normal individuals, there are often phlebectases in these sites just as there are on the nasal septum. We have not been impressed with these findings in our practice.

SUMMARY AND CONCLUSIONS

Ninety-seven patients with hemoptysis of undetermined origin were examined over a period of 9⅓ years.

Eighty-one of the above group (83.5 per cent) have been followed for periods ranging from 1 to 10 years.

Four of the 81 patients are known to be dead of causes unrelated to the hemoptysis.

Seventy-seven of the 81 patients followed (95 per cent) are known to be living at the present time.

Three of the known living patients, within 3 years of the original examination, had the bleeding explained on the basis of mitral stenosis, congestive failure, or primary pulmonary hypertension.

Although no cases of pulmonary carcinoma or tuberculosis are known to have subsequently developed in this series, it is probably a wise precaution to re-examine by x-ray all patients at intervals of a few months for 1 year after the original examination. Subsequent episodes of hemoptysis may require repetition of portions of the original study, although our experience would indicate that investigation of the pulmonary artery pressures might prove more productive.

The great majority (91.3 per cent) will continue in good health even though over 10 per cent may continue to have occasional episodes of hemoptysis. In an analogous situation in the urinary tract, with the same prognosis, the term "essential hematuria" is widely accepted. We feel there is equal evidence to support the terminology of "essential hemoptysis" in the cases under discussion.

REFERENCES

1. Jackson, C. L., and Diamond, S.: Hemorrhage From the Trachea, Bronchi and Lungs of Non-tuberculous Origin, Am. Rev. Tuberc. 46: 126, 1942.
2. Heller, R.: The Significance of Hemoptysis, Tubercle 27: 70, 1946.
3. Abbott, O. A.: The Clinical Significance of Pulmonary Hemorrhage: A Study of 1,316 Patients With Chest Disease, Dis. Chest 14: 824, 1948.
4. Levitt, N.: Clinical Significance of Hemoptysis, J. Michigan State M. Soc. 50: 606, 1951.
5. Souders, C. R., and Smith, A. T.: The Clinical Significance of Hemoptysis, New England J. Med. 247: 790, 1952.
6. Douglass, B. E., and Carr, D. T.: Prognosis in Idiopathic Hemoptysis, J. A. M. A. 150: 746, 1952.
7. Moersch, H. J.: Clinical Significance of Hemoptysis, J. A. M. A. 148: 1461, 1952.
8. Carr, D. T., and Douglass, B. E.: Hemoptysis, M. Clin. North America 38: 945, 1954.
9. Smidt, C. M.: Haemoptysis, Acta otolaryngol. 47: 265, 1957.
10. Seppälä, A. J.: Clinical Significance of Hemoptysis, Acta otolaryngol. 47: 172, 1957.
11. Falk, A.: Nonmalignant, Nontuberculous Hemoptysis in the Older Age Group, Geriatrics 12: 360, 1957.

DISCUSSION

DR. RODOLFO HERRERA, Guatemala City, Guatemala.—There is a disease called endemic hemoptysis or paragonimiasis which is quite common in Asia. Besides the fact that it was first discovered in a tiger in Amsterdam in 1877 there are two interesting things about this disease, which is caused by a fluke, *Paragonimus westermani*.

First is the fact that it has been reported in some parts of Latin America and in North America in United States Naval personnel. Second is the fact that the larvae of this parasite pass through the duodenal wall and then through the diaphragm and into the lungs, where they give rise to bloody sputum.

Similar life cycles exist in other more common parasites, such as Ascaris, Uncinaria, and the larvae are occasionally found in the sputum. The chest roentgenogram is usually negative at the time of the first bloody sputum, although a few days later it may show minimal areas of soft density which disappear spontaneously very rapidly. This is sometimes called tropical pulmonary eosinophilia in the English literature.

The point which I want to make is that in order to pin the diagnosis of idiopathic hemoptysis on a patient we should probably have negative studies of sputum and stool in search for parasites, in addition to the list of negatives given by Drs. Barrett and Tuttle in their very interesting paper.

DR. R. LEONARD KEMLER, Hartford, Conn.—To confirm the second point in Dr. Barrett's paper, we have had occasion to study a patient over a period of 22 years. This girl was a student nurse at the time when hemoptysis first occurred, and she had, in the 22-year period, a total of ten bronchoscopy studies done by various examiners, as well as twelve bronchograms. At no time was the etiology of the hemoptysis determined. The patient was offered a middle lobectomy 2 years ago, following bronchoscopy which showed blood coming from the right middle lobe orifice. She refused. One year ago, after the twelfth bronchogram was made, definite bronchiectasis was evident, this time in the right middle lobe, and the patient has had a right middle lobectomy in the past year.

The pathologic examination definitely proved the bronchiectasis in the right middle lobe.

DR. DUANE CARR, Memphis, Tenn.—There is one entity particularly prevalent in our section of the country for which one might well be on the lookout, and that is the broncholith, or bronchial stone. In an area in which histoplasmosis is endemic, there are a great many calcified nodes that are closely associated with the trachea and bronchial tree, including the almost uniformly demonstrable azygos node, as we call it, at the right side of the trachea. In time these may erode into a bronchus and may be expectorated, often being accompanied by hemoptysis for which no other cause can be found.

Obtaining the history of these is somewhat amusing at times. These patients frequently will recall, if prodded, that they indeed spat up what they thought was a piece of a tooth filling or a grain of sand, but not finding any absent fillings, they dismissed it from their minds. You have the diagnosis immediately from the history alone.

Some bronchial stones, or casts, actually form within the bronchi themselves as a result of long-standing inspissated pus, which becomes so dry and so hard that it finally calcifies and forms actual casts of the tracheobronchial tree or segments of it. These you find as staghorn stones, very much like those one finds in the pelvis of the kidney. Sometimes they can be seen at bronchoscopy. When not visible by bronchoscopy, it is not unknown to be able to spot them by careful perusal of serial x-ray films.

It is just one more entity to remove from those that one must designate as ''hemoptysis, cause unknown.''

DR. THEODORE R. HUDSON, Chicago, Ill.—Dr. Barrett showed one slide in which the presence of varicosities about the upper lobe orifices had been hypothecated. I can verify this in the case of a young woman who had a violent hemoptysis, and in the orifice of the left upper lobe I could see on bronchoscopy a wormlike, glistening mass which pulsated. I couldn't believe my senses, and I bronchoscoped her 2 weeks later with 2 other people present to look in with me. The same thing was seen again, looking just the same as it had before.

This was a varicosity, as shown by removal of the left upper lobe. This paper gives me a nice new term to put on the insurance forms. I am sure that the insurance people will accept ''essential hemoptysis'' more readily than they will ''hemoptysis, etiology undetermined.''

DR. TUTTLE (Closing).—I had nothing much to do with this paper, except that I bronchoscoped a number of these patients, and I coined the term ''essential hemoptysis.'' Dr. Barrett is to be credited with all of the work, which was prodigious. We sent out many follow-up letters and called many physicians in order to accomplish this study.

I think it is interesting that relatively few of these patients developed carcinoma. In fact, none in this series did, although there was 1 in the previous group that did after a period of two years. I think that we must not release this to the internists, because if we do, we will miss many carcinomas, and I think that is the one essential fact that must be brought out—that when bleeding occurs, bleeding should be traced, just as it is in the kidney.

The term ''essential hematuria'' has been known for many years. It was known when I was a student, and that was many years ago, and it is still known. And now we have recoined it for this phenomenon which occurs in the lung. But we still must trace it down, and so I would say on this whole subject, "Carry on, stout fellows!"

LIGATION AND DIVISION OF THE BRONCHUS IN THE SURGICAL TREATMENT OF CAVITARY TUBERCULOSIS

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AUTO-OCCLUSION of the bronchus occurs in the natural course of tuberculosis as an inconstant but very fortunate event. Many provocative concepts have been offered on its significance in cavity healing. Sudden and dramatic cavity closure occurred in unpredictable ways under the influence of pneumothorax, thoracoplasty, and even phrenic nerve paralysis. The credit that belonged to bronchial occlusion as the essential common denominator among these successful cases was bestowed liberally upon the various collapse measures by their enthusiastic proponents.

The importance of bronchial occlusion became obscured in later years with the popularity of resection therapy for pulmonary tuberculosis and, while accepted modern concepts of treatment have proved adequate for the vast majority of patients, there remains a significant group of patients for whom no surgical solution exists.

The purpose of this presentation is to record our experiences with 25 cases of advanced cavitary tuberculosis treated by operative bronchial occlusion.

HISTORICAL BACKGROUND

Anatomic, Bacteriologic, and Pathophysiologic Concepts.—

The concept of operative occlusion of the draining bronchus in cavitary tuberculosis evolved from basic studies on atelectasis. Clinical observations on ateletasis in tuberculous lungs and investigations on the behavior of tuberculous cavities and the role of their draining bronchi provide fundamentals essential to the logic of our thesis. Extensive bibliographies on the study of atelectasis have been compiled by many authors, notably by Coryllos[20] and Churchill.[20a] Selected references have been made to these and other studies, as they applied particularly to the development of operative bronchial occlusion in the treatment of tuberculous cavities.

The clinical acceptance of concepts developed experimentally frequently must await emotional or technical advances. In 1844 Mendelssohn[1] showed experimentally that bronchial obstruction caused atelectasis, and in 1879 Lichtheim[2] occluded bronchi in rabbits with sticks of lamenaria and stressed not only the importance of bronchial obstruction in lung collapse but also the role of the blood in the absorption of air distal to bronchial obstruction.

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Nevertheless, numerous theories on atelectasis continued to appear in the literature. Elliott and Dingley[3] in 1914 challenged the widely accepted concept of W. Pasteur[4, 5] in England that paralysis of the intercostal muscles and diaphragm was primary in the cause of atelectasis and pneumonia. These authors recognized that bronchial obstruction by retained secretions caused atelectasis and recommended cough and expectorants in its treatment. The wisdom of this concept became obvious clinically only after the adoption of bronchoscopic aspiration in the late 1920's. In 1928 Lee and his associates[6] presented very convincing experimental proof of the obstruction theory of atelectasis.

The popularity of pneumothorax and thoracoplasty in the 1920's aroused much interest in the possible effects on tuberculosis of spontaneous or induced atelectasis. An experimental approach to the pathophysiology of therapeutic pneumothorax by Andrus[7] in 1925 involved the collapse of one lung in dogs by bronchial ligation. The microscopic appearance of the lung after several months was one of passive vascular congestion and a dense cellular stroma which seemed to be composed of alveolar cells and many fibroblasts. During the same year, Gardner[8] reported on the pathology of artificial pneumothorax in tuberculosis. He observed that fibrosis in collapsed tuberculous lung was greatly in excess of that in an uncompressed tuberculous lung and suggested that the fibrosis might be accelerated or stimulated by lymph stasis. More important than this to our present thesis, he made reference to the failure of miliary tuberculosis in man to localize in collapsed lung tissue.

Van Allen and Lindskog[9] in 1930 contributed basic understanding to the mechanics of atelectasis with their discovery of intralobar collateral ventilation in dogs. They showed that atelectasis occurred when lobar bronchi were occluded, whereas atelectasis failed to occur when the occlusion was at the segmental level in otherwise normal lungs. Collateral ventilation was found to be present in normal respiration, being a delicate mechanism activated by a pressure differential of only a few millimeters of water. The presence of collateral ventilation in human lungs was confirmed in 1948 by Baarsma.[10] Van Allen[11] reported further in 1932 that patchy or lobular atelectasis will follow obstruction of small bronchi, provided that collateral ventilation has been suppressed by previous inflammatory thickening of the alveolar septa. An additional feature of collateral ventilation was provided in 1931 by Adams and Livingstone,[12] when they discovered that collateral ventilation occurred between lobes when interlobar fissures were not complete. The importance of this finding to bronchial ligation will be discussed later.

Phthisiologists presented divided opinions on the effects of atelectasis on pulmonary tuberculosis. Some observed deleterious effects while others considered atelectasis to be beneficial. Habliston[13] in 1928 cited the marked increase in negative intrapleural pressure following massive lung collapse and recommended artificial pneumothorax to relieve the resultant cardiac displacement and associated symptoms. Jacobaeus and Westermark[14] in 1930 and E. E. Glenn[15] in 1931 reported on the deleterious effects of atelectasis. The latter author noted that, following lobar atelectasis, cavities sometimes re-opened in ipsilateral lobes, presumably because of the more negative intrapleural pressure. The treatment suggested was artificial pneumothorax.

Favorable clinical effects of atelectasis on the course of pulmonary tuberculosis were described by Packard[16] in 1928, Hennell[17] and Korol[18] in 1931, and by Zavod[19] in 1938. The major contributions by Coryllos and by Adams on this concept will be reviewed.

The exhaustive studies made by Coryllos during the late 1920's and 1930's added greatly to our knowledge of cavitary tuberculosis, especially of the role of the draining bronchi, and the clinical importance of bronchial occlusion and atelectasis. Coryllos and Birnbaum[20] reported in 1928 on obstructive massive atelectasis of the lung, and noted that complete bronchial obstruction or lung compression always was present. They stated that artificial pneumothorax might be palliative, but was not therapeutic, and proposed bronchoscopic aspiration as the treatment of choice. In a later report in 1929, Coryllos[21] described the circulation of atelectatic lung and noted that ischemia was proportionate to the degree of lung collapse, that circulation and ventilation were parallel functions. In studies on pneumonia he observed that the fate of the lung after bronchial obstruction depended upon the microbes infecting the obstructing mucus,[22] and confirmed earlier work concerning absorption of gases from obstructed parenchyma by the circulating blood [23]

Coryllos and Ornstein[24] summarized their concepts in 1938. They attempted to correlate pathologic features of the draining bronchi to the seemingly erratic behavior of cavities[25-30] the usual oblique entry of draining bronchi through the cavity wall favored temporary bronchial obstruction because of compression as the cavity distended, inflammatory changes in the congested bronchial walls and tuberculous destruction of supporting cartilage rings, in the presence of inspissated mucus and blood, permitted temporary bronchial collapse and a check valve mechanism[31, 32] and set the stage for successful fibrous tissue obliteration and permanent bronchial occlusion and cavity healing, the passive vascular congestion attendant upon subsequent atelectasis resulted in tissue hypoxia, which in turn stimulated fibrous proliferation (likened to Volkmann's ischemic contracture) [33] They postulated that permanent atelectasis, as with thoracoplasty, accounted frequently for successful cavity closure since the proliferation of fibrous tissue in distorted bronchi was stimulated by an ischemic environment and permanent bronchial occlusion occurred, whereas pneumothorax failed frequently to accomplish cavity closure since the maintenance of collapse and ischemia were intermittent Reference to the stimulating effect of tissue hypoxia on fibrous tissue formation was made in 1930 by Leriche and Policard [34]

Coryllos and Ornstein included, in their report, studies on the bacteriology of tuberculous cavities To refute many previous reports of almost universal secondary bacterial contamination, it was possible by careful technique to demonstrate sterility of open cavities, except for the tubercle bacillus Coryllos had suspected that this was true, since serious suppurative complications had not been observed following cavity closure that occurred spontaneously, or by virtue of imposed collapse measures, such as thoracoplasty Coryllos concluded· "These bacteriologic findings are of considerable practical importance In fact, if the danger of obliteration of the draining bronchus is removed, there is no reason why we should not try to obtain it surgically, especially in cavities in which all other means of collapse, including thoracoplasty, have failed "

Simultaneous with the work of Coryllos during the 1930's, W E. Adams was investigating the effects of bronchial occlusion Adams, Van Allen, and Livingstone[35] reported on the response of bronchi to thermal injury and to silver nitrate cauterization, and observed the possibility of creating fibrous bronchial occlusion by these methods A safe and reliable method for closing large bronchi in dogs by endoscopic application of silver nitrate solution was suggested by Adams in 1933 [36] Aware of the beneficial effect of atelectasis on pulmonary tuberculosis, Adams and Vorwald[37] created lobar atelectasis in dogs by this technique and demonstrated, by gross and microscopic examinations, the beneficial effects of atelectasis on miliary tuberculosis, as well as the protective influence of established atelectasis against tubercle bacilli administered intravenously The effects of atelectasis on tuberculous lesions, produced endobroncially and subpleurally, also were described In the latter instances bronchial secretions were increased and complete bronchial occlusion with silver nitrate was difficult to accomplish They reported on the technique applied in 4 human cases in which complete bronchial occlusion was not obtained, apparently because of the copious bronchial secretions This obstacle to complete bronchial occlusion by cauterization was overcome by Escudero and Adams,[38] in 1938, when they performed bronchial ligation in dogs and accomplished healing of experimental tuberculosis in atelectatic lobes, while the tuberculous lesions progressed in aerating lobes in the same animal Kawabata[39] reported on the protective effects of induced atelectasis on hematogenous tuberculosis in rabbits in 1938

The vascular changes caused by induced atelectasis were described by Adams[40] as an increased vascularity, in the nature of a passive congestion rather than an active hyperemia Fibrous tissue proliferation in the atelectatic lung was considered insignificant in amount compared to the marked degree of fibrosis seen in infected atelectatic lobes The favorable effects of atelectasis on clinical tuberculosis were reported by Adams and Singer in 1935 [41]

The introduction in the late 1930's of transpleural decompression of cavities, and the interest aroused by investigations in cavitary dynamics, led naturally to a transcavitary attack on the draining bronchus to effect cavity closure. Coryllos and Ornstein[21] described unsuccessful attempts at transcavitary bronchial occlusion with sclerosing agents, electrocoagulation, and by the implantation of pedunculated muscle. Davidson[42] mentioned the use of a special telescope designed to locate and coagulate the draining bronchus. The various concepts were appealing, but the methods generally were not successful.

The lead provided by Escudero and Adams,[38] in using a direct surgical approach to bronchial occlusion by ligation, apparently was lost in the new popularity of resection therapy, and the untimely death in 1938 of Dr. Coryllos, who was the greatest proponent of this concept. In his monograph published in 1937 on The Surgery of Pulmonary Tuberculosis,[13] Coryllos stated that ". . . the key to the treatment of tuberculosis cavities is not to be looked for in their walls, but in their bronchial outlets. Therefore, our efforts must tend to the definite obliteration of these bronchi. Unfortunately, notwithstanding persistent research, I have not yet been able to find a procedure by which we could locate our intervention to the closure of these bronchi. Let us hope that we may succeed some day."

Although attempts at direct surgical approach to bronchial occlusion were abandoned for several years, many phthisiologists, familiar with the work of Adams, have tried to accomplish bronchial occlusion endoscopically. The senior author of this report (J. M. C.) was among these and was successful on several occasions in converting bronchial stenosis to temporary bronchial occlusion, with a few eventual good results. In 1940 Crafoord and Frenckner[44] described a successful clinical case of bronchial cauterization with silver nitrate. Their patient had developed bronchiectasis beneath a thoracoplasty and had positive sputum. Revision thoracoplasty was considered to be not appropriate in these circumstances. Although a tiny bronchial opening persisted after cauterization, the sputum converted and the patient remained well 2 years later. Melfi, Schwerlich, and Tamborini[15] reported also on the success of endobronchial treatment of pulmonary tuberculosis.

Since the foregoing experiments and conclusions were made in the pre-chemotherapy era, the question arises as to whether pathologic changes have occurred with chemotherapeutic agents that would be significant to operative bronchial occlusion. Auerbach, Katz, and Small[46] reported that stretopmycin induced a process of cavity healing different from that which occurred prior to the use of this drug. Reduction in perifocal reaction, thinner cavity wall, and lining of the bronchocavitary junction with squamous columnar epithelium, which extended for varying distances onto the cavity wall, were the major observations. Auerbach[47] observed that, in the era before chemotherapy, "closed healing" was by far the most frequent mechanism of cavity closure, occurring as the result of apposition of granulating surfaces of the ulcerated bronchus at the bronchocavitary junction, with eventual fibrous obliteration. Under the influence of chemotherapy, "open healing" occurred more frequently, with cavity inspissation and re-epithelialization and continued patency of the bronchocavitary junction. Thompson[48] reported 9.6 per cent incidence of "open healing."

The implications of these findings convey importance to studies on the pathogenicity of tubercle bacilli remaining in inspissated cavities. The respiratory metabolism of the tubercle bacillus in inspissated cavities had been studied by Novy and Soule[49] in 1925, and by Loebel, Shorr, and Richardson[50] in 1930. D'Esopo[51, 52] reported in recent years that such organisms were nonviable in 85 to 95 per cent of resected lesions and stated that there is no general agreement that these bacilli are, in fact, dead. The tuberculostatic or tuberculocidal influence of acidic necrotic debris in inspissated cavities was the subject of similar investigations by Dubos.[53] From the practical standpoint, ligation and division of the draining bronchus produces an unfavorable environment for the tubercle bacillus by causing tissue hypoxia and by retaining toxic necrotic debris within cavities.

The blood flow in dog lungs, made atelectatic by bronchial ligation, was reported by Bjork and Salen[54] in 1950. Blood flow through the atelectatic lung decreased progressively during the first month, until practically no blood passed through. Peripheral arterial desaturation was present immediately and returned gradually to normal as the blood flow reduced in the collapsed lung. No decrease in size of the pulmonary artery was noted. The vascular block was presumed to be in the capillary bed.

Whereas the report of Bjork and Salen deals with atelectasis and tissue hypoxia, factors considered beneficial sequelae of bronchial ligation, Hanlon, Scott, and Olsen and their co-workers[55] reported on the deleterious effects on experimental tuberculosis of pulmonary artery ligation. The mechanism of enhanced growth of tubercle bacilli under these circumstances lies in the fact that such lungs become perfused with highly oxygenated systemic blood through enlarged bronchial arteries. In a negative sense, therefore, these studies substantiate the virtues of bronchial ligation and division in the treatment of pulmonary tuberculosis. Further reference to ligation of segmental branches of the pulmonary artery will be made in our discussion.

Concepts on bronchial occlusion, similar to those developed in this country, received passing attention almost simultaneously in Europe. Jacquerod[57] in France, on the basis of his studies on tuberculous cavities, voiced the later conclusions of Coryllos, when he stated in 1924 that "when surgeons are able to accomplish permanent closure of the draining bronchus, the problem of closure of tuberculous cavities will be solved."

Nissen and Lezius, when assistants of Sauerbruch in Germany, succeeded in 1932 in occluding bronchi in dogs and observed that the lung was transformed to a fibrous mass after 3 months.[57] Twenty years later, the same two surgeons reported in Germany on bronchial ligation and division in 16 clinical cases of advanced cavitary tuberculosis.[58] Their conclusions on selection of patients, operative technique, various essential precautions and clinical results, are very comparable to our own conclusions, arrived at without knowledge of their work. In his excellent book on lung resection, published in 1953, Lezius[59] devoted a short section to bronchial ligation and division, with operative technique and important bronchocavitary anatomy beautifully illustrated.

Bogush, in Russia, impressed with the results of Nissen and Lezius, began to perform ligation and division of the bronchus in 1953. By 1957, he and his associates were able to report excellent results in 50 clinical cases of advanced cavitary tuberculosis.[60, 61] Conversion of sputum and cavity closure occurred in 43 patients, cavities remained open in 5 patients, and 2 patients died with contralateral pneumonia. The general conclusions of this report also are in agreement with our own. Margulis[62] reported in Russia, in 1957, on successful control of hemorrhage from a cavity by bronchial ligation and division in a patient who could not have tolerated more extensive methods of treatment. A similar case will be described in this presentation.

The American medical literature to our knowledge contains no previous report on bronchial ligation and division in the treatment of cavitary tuberculosis. The 25 cases to be presented comprise our total experience with this operation, the first having been performed in 1948.

SELECTION OF CASES

The decision to perform bronchial ligation and division was made most often on the basis of a combination of unfavorable features of cavitary tuberculosis. Many patients in this group obviously were beyond consideration for standard resection and collapse procedures. These had multiple cavities involving one or more lobes, often bilaterally, and over the years had healed diffuse parenchymal disease, now inconspicuous, at the expense of much functioning lung tissue. Several were thoracoplasty or pneumothorax failures, sometimes having been complicated by bronchopleural fistula and empyema. Marked reduction in pulmonary function and organism resistance to the major chemotherapeutic drugs were constant features of this group of tubercular relics, several of whom are present in every sanatorium, preparing to succumb eventually to their disease.

The group of patients just described comprised 15 of our 25 cases. Five among these were considered preoperatively to be suitable candidates for resection and thoracoplasty procedures. At operation the decision was made to perform ligation and division of the bronchus when the true extent of the disease process became apparent, and the concept of the proposed operation became untenable. For example, when the proposed operation for cavitary disease was upper lobectomy, superior segmental resection of the lower lobe and thoracoplasty, and extensive fibronodular disease was discovered in the middle and basilar segments, the proposed operation then assumed a high complication risk that was unacceptable to these patients. Pneumonectomy for them was unsuitable because of contralateral cavitary disease, or a functionally inadequate lung. Thoracoplasty, to be successful, would have had to be extensive and too demanding on pulmonary function. The surgical alternative for these patients was to subject them to an unreasonable risk, or to abandon hope and do nothing.

Three patients not included in this category, although similar in clinical features, were subjected to ligation and division of the bronchus as "desperation measures" (Cases 3, 10, and 12). They survived postoperatively 1 month, 2 months, and 2 months, respectively. We considered it as unlikely that the operations altered the inexorable courses of their disease.

Ligation and division of the bronchus was performed on three occasions when the proposed resection could not technically be accomplished. In Cases 1 and 4, right upper lobectomy beneath a thoracoplasty was attempted. These carnified lobes were fused to the chest wall and to adjacent lobes The organized and calcified tissues surrounding the hilar vessels defied dissection and identification. The bronchus in each case was secured with great difficulty, and was ligated in 1 case and divided in the other. Case 7 also was proposed for a right upper lobectomy for control of hemorrhage from inactive tuberculous bronchiectasis and calcification. Uncontrollable bleeding was encountered wherever the dissection was directed to mobilize the adherent lobe. The hilar structures therefore were approached posteriorly and the posterior segmental bronchus was ligated and divided. The pulmonary hemorrhage was controlled completely by this maneuver.

Two female patients became candidates simultaneously for bronchial ligation and division when one refused resection beneath a left thoracoplasty, and the other refused a thoracoplasty that would have been essential following the recommended right upper lobectomy (Cases 13 and 14). Each consented to the proposal of ligation and division. Operated upon the same day, each had an excellent clinical result.

Case 6 was unique in that the cavitary left lung contained extensive fibrosis, the result of radiation therapy following radical mastectomy for breast carcinoma. Upper lobectomy, superior segmental resection, and extensive thoracoplasty were considered hazardous and too demanding upon the markedly reduced pulmonary function Old contralateral disease precluded pneumonectomy. T[illegible] be and superior segmental bronchi were divided and a small posteric[illegible] was performed. An excellent result has extended almost [illegible]

The operative indications were debatable, in our opinions, only in Case 22. Bilateral upper lobectomy and thoracoplasty could have been justified for this patient. Realizing that there were multiple cavities in both upper lobes and scattered infiltrative and nodular disease in both lower lobe apices, we were concerned with avoiding space problems and preserving maximum pulmonary function. The unexpected and unfortunate outcome in this case remains unexplained.

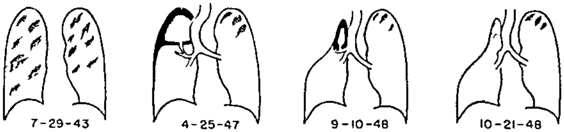
The factor of age was not an important indication in this series of cases, except in Cases 17 and 25. These patients were 66 and 75 years of age but, in spite of drug resistance, might have tolerated resection. The operative trauma and the potential complications were considered to be less with bronchial ligation and division. Similar reasoning might be applied to patients having cavitary tuberculosis, who have had relatively recent operations for carcinoma, with doubtful outcome. Psychotic patients incapable of cooperation, in whom immediate bacteriologic negativity is an important safeguard to other patients and personnel, logically are candidates also for this operation.

Experience gained from the diverse problems encountered in this series of 25 cases has enabled us to formulate certain rules and precautions in case selection, as well as in operative technique. For this reason we considered it essential to present each case in some detail, along with diagrams of representative roentgenograms of the chest.

CASE REPORTS

CASE 1.—(Fig. 1; P. O., 50, white male.) Onset 1943, with far-advanced disease in all lobes. Two-stage thoracoplasty in 1947 failed to close giant cavity. Upper lobectomy was planned. Bronchus to RUL ligated, when at thoracotomy on Sept. 11, 1948, a pneumonectomy was the only alternative. Operation successful. Death occurred 6 weeks later from amyloid uremia.

Comment: Successful. This first case of bronchial ligation accomplished cavity obliteration and sputum conversion. The bronchus should have been divided. Death unrelated to operation.



7-29-43
ADMISSION

4-25-47
(TOMOGRAM)

9-10-48
7 MONTHS POST-
THORACOPLASTY

10-21-48
6-WEEKS POST-
LIGATION
R.U.L. BRONCHUS

Fig. 1.

CASE 2.—(Fig. 2; M. C., 40, white female.) Onset 1942, bilateral apical. Cavities RUL, LUL, and superior segment LLL in 1952, with drug resistance and pulmonary insufficiency. At operation on April 22, 1953, left upper lobectomy, superior segmental resection, and thoracoplasty was considered too hazardous. LUL bronchus divided, found to be completely occluded. Superior segmental bronchus and accessory subapical bronchus divided (see Fig. 29). Extraperiosteal Gelfoam plombage, ribs 1-4. Remains well after 7 years.

Comment: Successful. Auto-occlusion of LUL bronchus and accessory sub superior segment were interesting features of this case. The latter was divided along with the superior segment, possibly discouraging collateral ventilation.

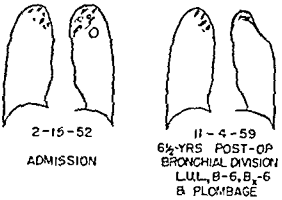


Fig. 2.

CASE 3.—(Fig. 3; M. K., 31, white female.) Onset 1941. Bilateral pneumothorax failed to close cavities in RUL and superior segment of RLL. Presented for surgery in 1953 as "desperation measure" with increasing parenchymal disease, bilobar cavities on right, drug resistance, uncontrolled fever to 103° F. daily, and marked ventilatory impairment. Cavity entered inadvertently, closed. Bronchopleural fistula and empyema fatal after 1 month.

Comment: Failure. Lung should have been mobilized in extraperiosteal plane over area of disease. We did not consider the complication to be condemning to operation performed on this patient with fulminating disease.

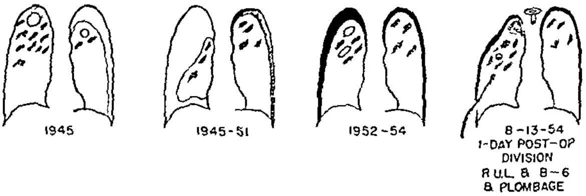


Fig. 3.

CASE 4.—(Fig. 4; K. W., 48, white female.) Onset 1949, with disease in all lobes, and a large cavity in a contracted RUL, persisting after 2 years of pneumothorax, and after plombage and thoracoplasty. Carnification of RUL and hilar structures defied resection on Nov. 6, 1954. RUL bronchus divided, as only alternative. Sputum converted. Remains well.

Comment: Successful case which demonstrates that the difficulties encountered in performing resection for thoracoplasty failure can be solved by bronchial ligation and division.

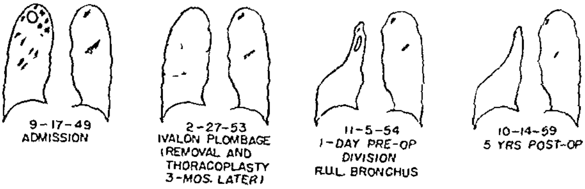


Fig 4.

CASE 5.—(Fig. 5; J. B., 41, white female.) Onset 1946, remission to 1950, when all lobes involved. Pneumothorax failure on right, controlled by thoracoplasty. Cavity developed in superior segment, LLL, and segmental resection planned. At operation on March

14, 1956, extension of disease into basilar segments indicated hazardous situation for segmental resection. Two divisions of B-6 divided. Sputa intermittently positive for 1 year, negative since then.

Comment: Eventual successful case. The entire superior segmental bronchus should have been divided. Cavity control could not be claimed for operation performed. Subsegmental bronchial ligation is ineffectual.

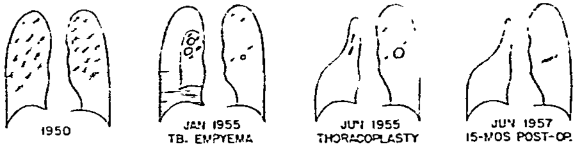


Fig. 5.

CASE 6.—(Fig. 6; M. L., 37, white female.) Onset 1936, with cavities RUL, LUL, lingula, and superior segment of LLL. All cavities closed after 4 years bilateral pneumothorax. Left radical mastectomy for breast carcinoma in 1954, followed by chest wall x-radiation. Cavities reopened LUL and LLL in 1955. Drug resistance, borderline pulmonary function, and contralateral disease indicated bronchial division. Operation on May 24, 1958. Sputa converted. Remains well.

Comment: Successful. Application of this operation to patients with recent carcinoma and radiation fibrosis is recommended.

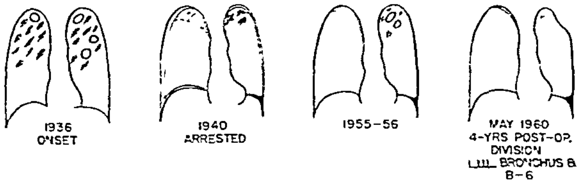


Fig. 6.

CASE 7.—(Fig. 7; G. A., 59, white male.) Stable, honeycombed disease RUL many years. Repeated hemoptyses late 1956-1957. Sputum negative. Hemogram normal. Lobectomy attempted on May 16, 1957. Lobe carnified; bleeding profuse. Posterior segmental bronchus led to major disease and was divided. Bleeding controlled. Unexpected degree of collapse indicated no collateral ventilation. Remained well 6 months, then died with acute leukemia.

Comment: Successful case which demonstrates application of bronchial division for pulmonary bleeding and to retrieve a technically difficult dissection problem.

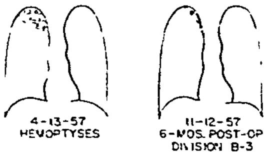


Fig. 7.

CASE 8.—(Fig. 8; Z. V., 23, white female.) Onset Puerto Rico 1951. Exacerbated in 1953. Presented in 1957 in New York City with cavities RUL, LUL, and LLL, and drug resistance. Planned bilateral resections and thoracoplasty. At operation on Aug. 16, 1957, extensive basilar disease indicated bronchial division as safer procedure. LUL and B-6 divided. RUL resected on Sept. 27, 1957. Remains well.

Comment: Successful case which demonstrates the change of operative plan upon discovering unexpected extent of disease, and use of bronchial division when pneumonectomy is contraindicated. Today we would perform also a selective extraperiosteal thoracoplasty.

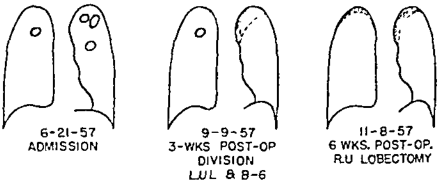


Fig. 8.

Case 9.—(Fig. 9; F. P., 45, Negro female.) Psychotic, syphilitic Negro woman developed bilateral disease in 1949. RUL resected 1954. Cavity in basilar segments of RLL in 1956. Left sanatorium against medical advice in 1957, returned 1958 with enlarged cavity, drug-resistant organisms, low pulmonary function. Bronchial division considered procedure of choice. At operation on April 11, 1958, cavity opened, filled with saline, and "bubbled" by anesthetist to identify communicating bronchi. B-9 and B-10 divided. Cavity remained open and bronchiectasis developed. Completion pneumonectomy in October, 1958.

Comment: Failure. Deliberate opening of the cavity to identify draining bronchi probably should not be done. We do not believe that basilar cavities are best treated by bronchial division, especially in the presence of lung distention following ipsilateral lobectomy.

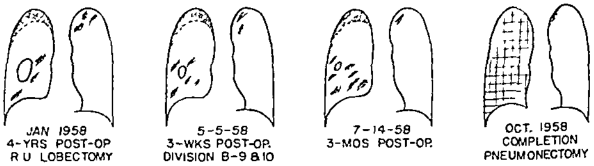


Fig. 9.

Case 10.—(Fig. 10; W. J., 40, white male.) Onset right apical disease in 1943. Disciplinary problem, failed to curtail activities and to take drugs. Accepted hospitalization in 1957, with RUL, LUL and LLL cavities, and old empyema, right. Organisms resistant. Thoracoplasty June, 1957. Marked impairment of pulmonary function. LUL bronchus and B-6 divided on April 16, 1958, as "desperation measure." Cavities closed and sputum converted. Cardiopulmonary failure was progressive and death occurred 10 weeks postoperative.

Comment: Failure. Successful cavity collapse was accomplished. We did not consider that the operation performed was responsible for death.

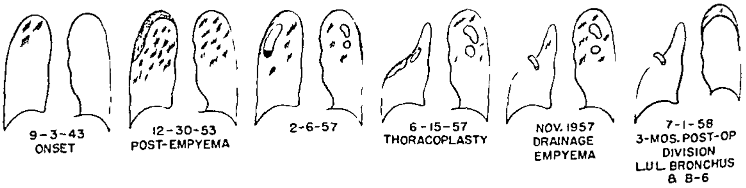


Fig. 10.

CASE 11.—(Fig. 11; A. R., 35, white female.) Onset LUL disease Puerto Rico 1950. improved after 1 year of pneumothorax and triple chemotherapy. Presented in New York City in 1956 with extensive disease, and cavities in RUL, RLL and LUL. Organisms resistant. Pulmonary function markedly reduced. Presented for surgical evaluation in 1958; bronchial division considered procedure of choice. On April 24, 1958, RUL bronchus divided. Lower lobe cavity extended into basilar segments. Cavity opened, filled with saline, and "bubbled" by anesthetist. B-6 and B-9 divided. RUL continues to ventilate, and both cavities remain open to present time. Opportunity still present for plombage or resection.

Comment: Failure. Demonstrates the virtues of simultaneous extraperiosteal thoracoplasty, as portrayed in Fig. 26. This should have been done in this case to obliterate channels of collateral ventilation. Probably B-10 should also have been divided.

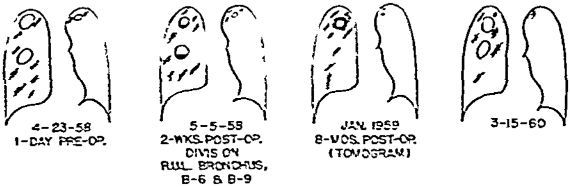


Fig. 11.

CASE 12.—(Fig. 12; M. P., 56, white male.) Syphilitic, diabetic, schizophrenic man, presented in 1952 with extensive bilateral disease. Cavity persisted in RUL. Personality precluded cooperation. Steady deterioration. Organism resistance by 1958. Bronchial division considered only possibility to retrieve desperate situation. RUL bronchus divided on June 20, 1958. Cavity entered inadvertently in extrapleural plane; closure with absorbable sutures. Proximal bronchial stump disrupted on fourth postoperative day. Empyema drained. Death unexpected on Aug. 30, 1958. Autopsy showed perforated gall bladder, general peritonitis, adequately drained empyema.

Comment: Failure. Lung mobilization should have been done in the extraperiosteal plane to avoid entering the cavity and to provide lateral collapse. In addition to operative complications, death was related to ruptured gall bladder and peritonitis.

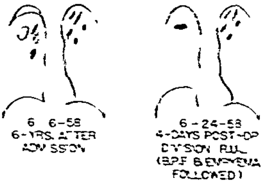


Fig. 12.

CASE 13.—(Fig. 13: H. F., 52, white female.) Chronic alcoholic. Small RUL cavity in 1949. Two large cavities by 1950. Thoracoplasty refused. Cavities closed intermittently. LLL cavity in 1951. Inferior alveolar ridge resected for carcinoma in 1954. Uvula excised for recurrence in 1956. Radical neck dissection in 1957. Meanwhile, cavities persisted. Bilateral resection and thoracoplasty refused. Consented to bronchial ligation and division. RUL and B-6 divided on July 16, 1958. Cavities closed. Superior segmental resection of LLL scheduled for January, 1959. Patient died that month of pulmonary embolus following repair of strangulated inguinal hernia.

Comment: Successful case. Refused resection and thoracoplasty. Death 6 months later was not related to operation.

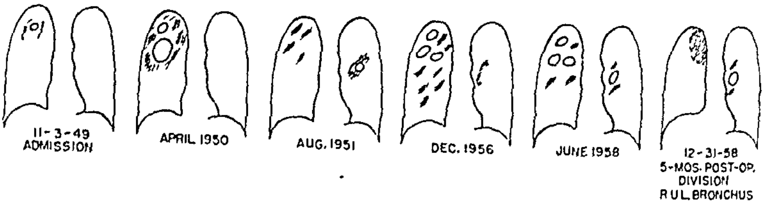


Fig. 13.

CASE 14.—(Fig. 14; E. J., 38, Negro female.) Onset in January, 1955. All lobes involved. Cavities in RUL and LUL, persisting during pneumoperitoneum and chemotherapy. Thoracoplasty on left in October, 1957. RUL resected in January, 1958. Resection beneath thoracoplasty for persistent cavities refused, but consented to bronchial division. LUL bronchus divided on July 16, 1958. Cavities closed and sputum converted. Remains well.

Comment: Successful case. Refused resection beneath thoracoplasty.

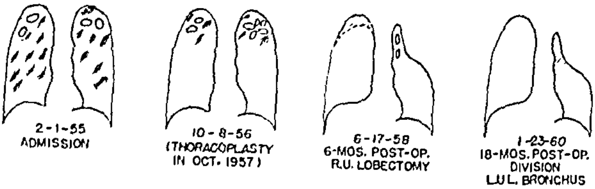


Fig. 14.

CASE 15.—(Fig. 15; W. H., 32, white male.) Minimal tuberculosis in 1944. Exacerbation bilaterally in 1955. Refused hospitalization until 1957. All lobes involved, with cavities in RUL, RLL, LUL, and LLL. RLL cavity closed by January, 1958. Pulmonary function borderline. Upper lobectomies, superior segmental resections, and thoracoplasty, bilaterally, considered too extensive. RUL bronchus divided on July 17, 1958, with effective cavity closure. Left thoracotomy on March 9, 1959. Apical-posterior segmental bronchus of LUL divided. The anterior and lingular segments were very large. To preserve maximum function of these segments, and to prevent or reduce collateral ventilation into the apical-posterior segments that might prevent their collapse, the anterior segmental bronchus was divided (see Fig. 28). B-6 also was divided. Cavities closed and sputum converted. Remains well.

Comment: Successful case of bilateral bronchial ligation and division. Today we would perform simultaneous selective extraperiosteal thoracoplasty, and ligate and divide prophylactically B-6, right, to ensure continued cavity closure in that segment.

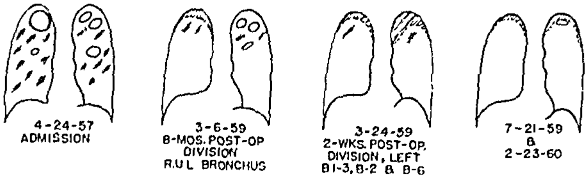


Fig. 15.

CASE 16.—(Fig. 16; W. G., 46, white male.) Onset 1955. Remained hospitalized. Multiple cavities RUL. Giant cavity RLL apex. LUL honeycombed. Sputum persistently positive. MBC, 39 L. per minute. VC, 42 per cent. TVC, 75 per cent in 3 seconds. Right lung performed 14 per cent of total ventilation. Fluoroscopy showed air-trapping in giant cavity. Arterial O_2 89 per cent breathing room air, and 93 per cent breathing oxygen. RUL bronchus and B-6 divided on Sept. 4, 1958. Sputum converted and has remained negative. Three months later, MBC was 43 L. per minute, and VC 77 per cent. Arterial oxygen saturation normal.

Comment: Successful case which demonstrates improved ventilatory and respiratory function. Today we would perform also a small extraperiosteal thoracoplasty to assist collapse and to discourage collateral ventilation.

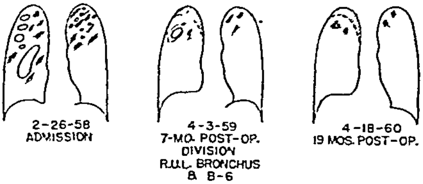


Fig. 16.

Case 17.—(Fig. 17; H. Z., 66, white male.) Onset October, 1956. Exudative disease in all lobes on right. Multiple cavities in RUL. Diaphragms flattened. Organisms resistant to major drugs in 1958. Elected to perform bronchial division because of age, poor pulmonary function, and organism resistance. RUL bronchus divided on May 11, 1959. Cavities closed and sputum converted.

Comment: Successful case, age 66. Advisable to perform simultaneous extraperiosteal thoracoplasty over apex.

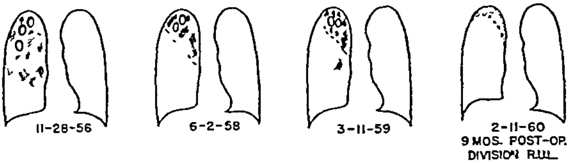


Fig. 17.

Case 18.—(Fig. 18; H. M., 58, white male.) History of pulmonary emphysema. Onset tuberculosis August, 1957. Dense exudative disease in RUL and apex of RLL. Minimal disease LUL. Some contraction of RUL occurred after 18 months. Ventilatory studies and blood gas analyses confirmed moderate emphysema. RUL bronchus divided on June 8, 1959. Cavities closed and sputum converted. Remains clinically well.

Comment: Successful case. Extraperiosteal thoracoplasty over apex advisable.

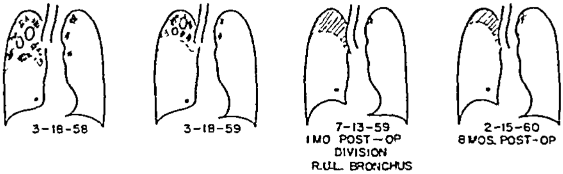


Fig. 18.

Case 19.—(Fig. 19; W. G., 49, Negro male.) Exudative disease in all lobes in 1954. Cavities persisted in contracted RUL. Left sanatorium against medical advice. Increased disease bilaterally in 1959. Pulmonary function markedly diminished. At operation on Sept. 16, 1959, because of incomplete major fissures and extensive middle lobe and basilar disease, decision made to divide RUL bronchus and B-6 as alternative to hazardous resection. Posterior thoracoplasty, ribs 2 to 5. Cavities closed. Sputum converted. Remains well.

Comment: Successful case. Not necessary to remove ribs.

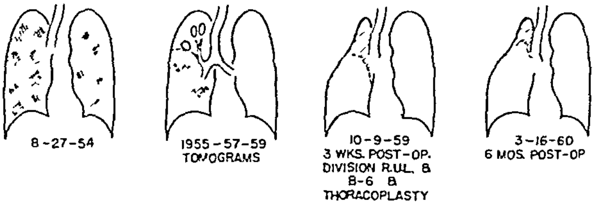


Fig. 19.

CASE 20.—(Fig. 20; E. S., 45, white male.) Onset 1951. Exacerbation 1956. Inadequate chemotherapy on these occasions. Diffuse disease in RUL, with contracted thoracic cage and retracted trachea. Sputum positive October, 1959; cavities in RUL and apex of RLL. Lobectomy and segmental resection planned. At operation, on Oct. 14, 1959, found extensive disease in RML and basilar segments, considered hazardous circumstances for resection. RUL bronchus and B-6 divided. Cavities closed and sputum converted. Discharged from hospital on thirteenth postoperative day. Septic course 3 weeks later, with abundant phlegm containing tubercle bacilli. RML infiltration presumed tuberculous pneumonia. Pneumonectomy was considered when, in January, 1960, the RML cleared, the sputum became nil and negative for tubercle bacilli. Subsequent course excellent.

Comment: Complicated but successful case. Illustrates point to not decide too quickly on basis of bizarre postoperative x-ray signs to accept failure and resort to resection.

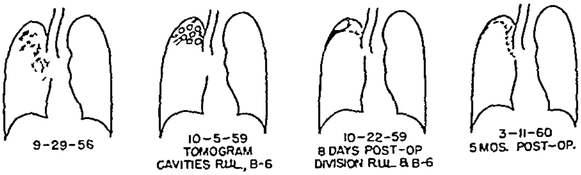


Fig. 20.

CASE 21.—(Fig. 21; V. D., 48, white male.) Onset 1947, all lobes. Two large cavities in LUL remained open following thoracoplasty in 1947. Apical-posterior and anterior segmental resections of LUL on Feb. 14, 1949. Sputum converted. Giant cavity RUL in April, 1958. Drug resistance present by April, 1959, and marked pulmonary insufficiency. Bronchial

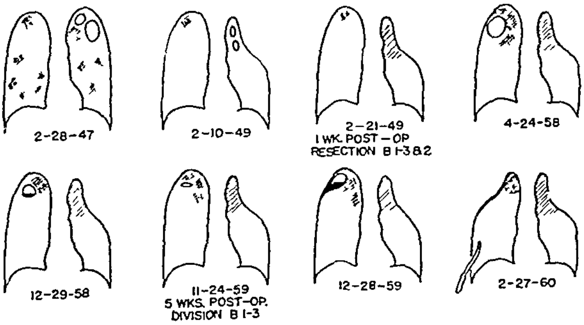


Fig. 21.

division elected as procedure of choice. At operation on Nov. 17, 1959, it was considered essential to preserve the very large anterior segment. The apical-posterior bronchus was divided. To prevent collateral ventilation, an "artificial fissure" was created between the apical-posterior and the anterior segments. Tuberculous empyema developed 5 weeks later, the cavity having ruptured through the "artificial fissure." Drainage and thoracoplasty done. An eventual good result is expected.

Comment: Failure. No attempt should have been made to create an "artificial intersegmental fissure." The lobar bronchus should have been divided and an apical extraperiosteal thoracoplasty performed.

Case 22.—(Fig. 22; M. N., 48, white female.) Discovered in 1947 to have hyperthyroidism, diabetes mellitus, and LUL tuberculosis. Thyroidectomy done. LUL cleared with chemotherapy but progressed in 1952 when diabetes was uncontrolled. Hemoptyses 1954-1955. Sputum positive 1957. Extensive parenchymal and cavitary disease both upper lobes in 1959. Nodular disease both lower lobes. Required 50 units insulin daily. Faced with resection and thoracoplasty bilaterally in a severe diabetic, LUL bronchus ligated, but not divided, on Nov. 9, 1959. Discharged from hospital 11 days later. Fatal hemoptysis at home on Dec. 18, 1959. Autopsy not done. Question remains whether hemorrhage arose from LUL or from a contralateral cavity.

Comment: Failure. The bronchus should have been divided and a relaxing extraperiosteal thoracoplasty performed.

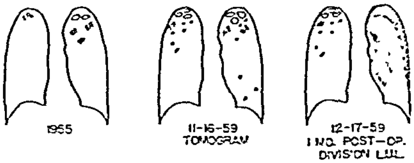


Fig. 22.

Case 23.—(Fig. 23; J. B., 49, white male.) Diabetic, chronic alcoholic. All lobes involved in 1951. Cavities in RUL, LUL, and apex of LLL. In spite of triple chemotherapy, cavities enlarged, and, in 1958, a cavity appeared in apex of RLL. Organisms resistant. Pulmonary function markedly reduced. On Jan. 18, 1960, LUL bronchus and its individual segmental bronchi were doubly ligated and not divided. B-6 also ligated. Five-rib thoracoplasty done. Cavities closed 8 days later, only to re-open 2 weeks later. Fatal hemoptysis occurred on Feb. 10, 1960. Autopsy showed hemorrhage from cavity in opposite lung. The doubly ligated bronchi had sloughed, and loculated empyema was present.

Comment: Failure. The bronchi should have been divided to permit bronchial retraction away from the hilum, and medial cavity to collapse. Not necessary to remove ribs.

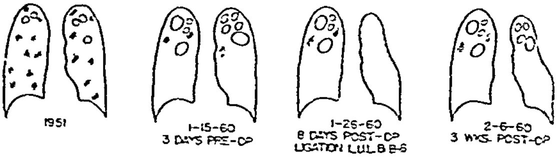


Fig. 23.

Case 24.—(Fig. 24; A. N., 35, white male.) Onset 1957 in Puerto Rico. Presented in New York City early in 1958 with RUL cavity. Disease progressed and drug resistance developed after 2 years. Both upper lobes contracted. Trachea distorted. MBC, 29 L. per minute. On April 22, 1960, RUL bronchus and B-6 divided. Periosteum elevated from ribs 1 to 4 posteriorly. Cavities closed. Too early for evaluation.

Comment: Operation tolerated well in spite of marked impairment of pulmonary function.

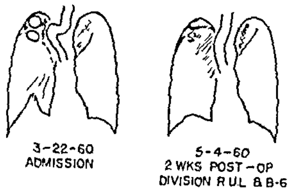


FIG. 24.

CASE 25.—(*Fig. 25; F. T., 75, white male.*) *Known to have scarring and calcific foci in RUL for many years. First clinical evidence of tuberculous activity in 1957.* Cavity RUL. *Sputum positive. After 22 months chemotherapy,* cavity closed and sputum converted. Cavity re-opened *in October, 1959,* sputum positive, organisms resistant. Advanced age and *resistant organisms indicated* bronchial division as procedure of choice. RUL bronchus *divided and* periosteum elevated from ribs 1 to 4 on April 26, 1960. Cavity closed. No sputum.

Comment: Successful case, 75-year-old patient. Effective circumferential cavity collapse.

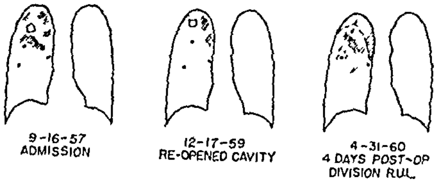


FIG. 25.

TECHNICAL CONSIDERATIONS

The Incision.—A standard posterolateral thoracotomy incision is extended sufficiently *high in the* interscapular region to permit performance of an extraperiosteal thoracoplasty, *if indicated. The pleural cavity* is entered through the bed of the fifth rib, or through the *fifth interspace if desired.*

Lung Mobilization.—Cases of long-standing, cavitary lesions often present a severe form of obliterative pleuritis. Under these circumstances, exposure of the lobar bronchus *can be difficult, since it is concealed by the* inflated, adherent lung. The hilar structures may be approached in either of three different planes: the *intrapleural plane,* the extrapleural plane, and the *extraperiosteal plane,* which becomes extrapleural as one approaches the mediastinum. Mobilization of *the* lung in the *intrapleural plane* can damage the parenchyma and produce small, but undesirable, alveolar air leaks. Therefore, mobilization of the lung in the extrapleural or the extraperiosteal *plane is preferable.*

Lung mobilization is hazardous when the inflammatory *reaction has been so* violent as to *obliterate the extrapleural* space and fuse the diseased lung to the periosteum and to the intercostal muscles. This finding usually indicates that the *cavity wall is immediately* subpleural. A persistent effort to dissect in this plane may prove disastrous for two reasons. First, the underlying cavity may be *inadvertently entered and, second, the* nutritional blood supply to the cavity wall or underlying lung may be interrupted. This consideration is extremely important when it is recalled that the bronchial *artery* is to be divided along with the bronchus.

Lung mobilization in one plane or another is desirable because it allows the diseased parenchyma to collapse when the bronchus is divided. Adequate collapse will tend to ensure the obliteration of intersegmental communications and thereby permit atelectasis to occur, with its beneficial effects on healing. We believe that these pathways between segments or lobes, at the bronchiolar or alveolar levels, if not obliterated, may provide devious routes for acid-fast bacilli to reach the tracheobronchial tree and for collateral ventilation to occur, and thus prevent the desired collapse.

When lung mobilization and hilar exposure can be accomplished easily through the intrapleural or extrapleural plane, it is likely that lung collapse can occur, since it is not prevented from doing so by chest wall adhesions. However, if the bronchial ligation and division is to be segmental or if it is to be lobar in lungs having incomplete major fissures, we believe that a selective, extraperiosteal thoracoplasty over the cavity area will ensure lung collapse by obliterating these potential, retrograde channels. Since extreme therapeutic collapse is not required, the deformity of the standard thoracoplasty can be avoided by leaving the ribs in place. This concept of "circumferential collapse" is portrayed in Fig. 26. In addition, increased negativity of intrapleural pressure, because of the imposed atelectasis, is obviated by extraperiosteal thoracoplasty, thereby protecting areas of disease in the ipsilateral or contralateral lung against mediastinal shift and overdistention.

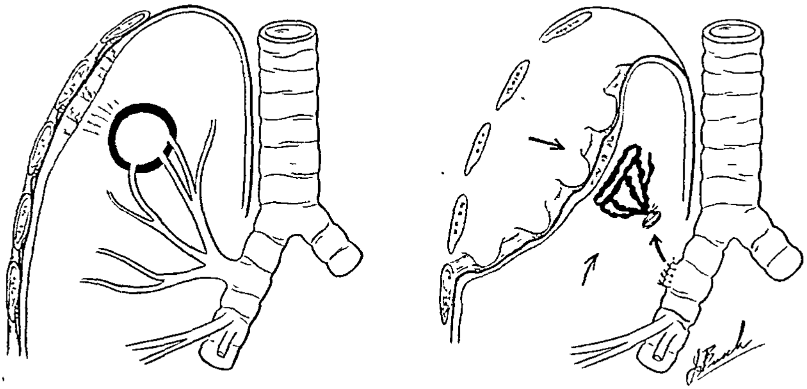


Fig. 26.—This drawing demonstrates the concept of "circumferential cavity collapse." *A*, The pleura adjacent to the cavity is adherent to the periosteum and intercostal muscles. Multiple segmental bronchi communicate with the cavity. *B*, Lung mobilization has been carried out in the extraperiosteal plane over the adherent zone to provide lateral cavity collapse, while preserving the chest wall collateral blood supply to the cavity. Recoil of the divided upper lobe bronchus provides, in addition to the lateral collapse, an accordion-like relaxation of the medial cavity wall.

The Hilar Dissection.—A well-padded Penrose drain is passed around the main bronchus. Traction on the main bronchus then permits easy and accurate identification of the desired bronchus or bronchi. The major bronchial arteries may be visualized, and branches to other lobes carefully preserved.

Division of Lobar Bronchi.—As soon as the proper bronchus has been identified and isolated, it may be divided. The proximal stump is closed with interrupted silk sutures and covered with viable tissue. The distal stump is doubly ligated with 1-0 silk, and allowed to recoil into the depths of the pulmonary parenchyma, enabling collapse of the medial wall of the cavity. It was reasoned that ligation of the distal stump was preferable to closure by interrupted sutures, since the latter might act as small wicks along which extravasation of cavity contents might occur (Fig. 27).

Division of Segmental Bronchi.—Segmental bronchi are divided at their origins between doubly ligated 1-0 silk ligatures placed 1.5 cm. apart (Figs. 28-29). Segmental bronchi in the left upper lobe usually are concealed by several branches of the pulmonary artery. We have not seen adverse effects from ligating one or two of these vessels in approaching the underlying bronchus. Collateral ventilation must be dealt with when ligation and division are at the segmental level. Figs. 28 and 29 suggest methods of management in conjunction, ideally, with extraperiosteal "circumferential collapse," as shown in Fig. 26.

Pleural Drainage.—One intercostal tube is placed in the pleural cavity for purposes of suction drainage and re-expansion. If care has been exercised in mobilizing the lung and no significant air leaks are present at the time of closure, the tube can be removed the following day and the patient allowed out of bed.

RESULTS OF OPERATION

While it is customary to judge a surgical procedure on the basis of results obtained, the presentation of charts and graphs in this report would shed no light on the merits or faults of bronchial ligation and division as we envision it today. We believe that we have learned much about case selection, and have developed concepts on the proper conduct of the operation, all at the expense of the 25 unusually diverse cases in this original report. The application of our present concepts to future cases will determine the worth of this operation.

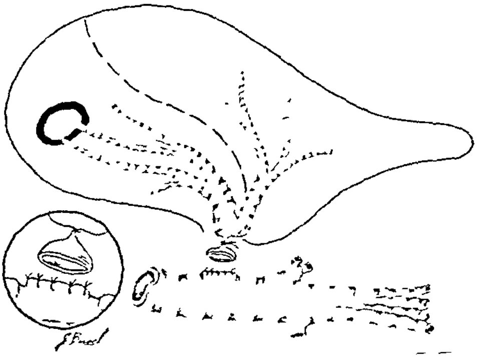


Fig. 27.—The operator's view of the posterior aspect of the right upper lobe, which is retracted anteriorly. The entire lobar bronchus has been divided, to prevent collateral ventilation from the uninvolved anterior segment. The details of proximal bronchial suture and distal bronchial ligation are shown.

Three patients were accepted for bronchial ligation and division as a "desperation measure" (Cases 3, 10, and 12). Each was considered an operation failure, although without operation an early fatal outcome was certain. Two died with bronchopleural fistula and empyema, while the third died with pulmonary insufficiency. The operation did not appear to alter his progressive deterioration.

Two other fatal results were Cases 22 and 23. Each of these had fatal pulmonary hemorrhages, 1 month and 3 weeks postoperatively. The former patient, in our present concept, should have had a relaxing extraperiosteal thoracoplasty, in addition to bronchial division. Her clinical course had been excellent up to the day of death. The site of hemorrhage could not be determined without autopsy. The other patient bled from a contralateral cavity, proved at autopsy.

Three additional deaths occurred from causes unrelated to the operation. Case 1 had cavity collapse and sputum conversion, but died after 6 weeks with amyloid uremia. Case 13 also had an excellent operative result, with cavity closure and sputum conversion, but died after 6 months with a pulmonary embolus following herniorrhaphy. Case 7 had successful bronchial ligation and division for pulmonary hemorrhage. He died with leukemia 6 months later.

Three patients still living were obvious operation failures. Case 9 required completion right pneumonectomy for middle and lower lobe bronchiectasis, persistent basilar cavity, and positive sputum. Previous to division of B-9 and

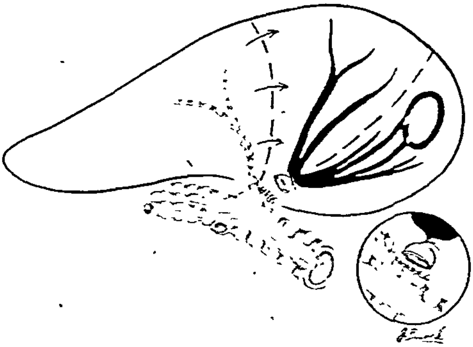


Fig. 28.—The operator's view of the posterior aspect of the left upper lobe, which is retracted anteriorly. The cavity is located in the apical-posterior segment. This bronchus and the adjacent anterior segmental bronchus have been divided. The lingular segments have been preserved. While collateral ventilation can occur into the anterior segment from the lingula, it was reasoned that collateral ventilation would not traverse this blocked segment (see Case 15).

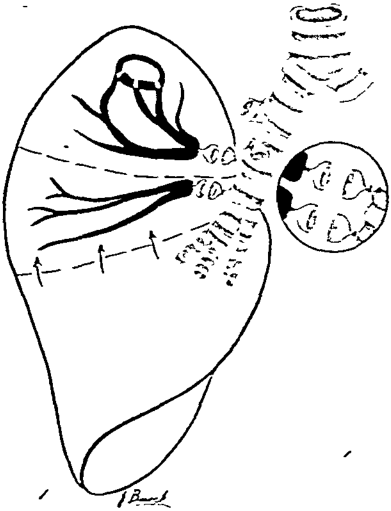


Fig. 29.—The right lower lobe is shown with a cavity in the superior segment. (The upper and middle lobes have been removed for clarity.) The superior segmental bronchus and an accessory sub-superior bronchus have been ligated and divided. The fortuitous presence of the latter provides an interposed segment which can aerate only collaterally from the basilar segments. Case 2 presented this situation in the left lower lobe.

B-10 the patient had had a right upper lobectomy. In retrospect, bronchial division performed in the remaining markedly overdistended lung without relaxing thoracoplasty was doomed to failure. Case 11 has persistent cavities and positive sputum, both of which might have been averted had an extraperiosteal thoracoplasty been combined with the bronchial division procedure. Case 21 developed bronchopleural fistula and empyema as the result of an ill-conceived attempt to preserve the anterior segment of the right upper lobe by creation of an artificial intersegmental fissure. Each of these failures is avoidable according to present concepts.

The remaining 14 patients, in addition to the 3 who died from unrelated causes, had excellent results, with cavity closure and sputum conversion.

In summary, bacteriologic negativity and cavity closure were accomplished in 17 cases, and 1 patient was negative preoperatively (Case 7). Of the 6 patients not converted, 3 are dead, 1 is negative following pneumonectomy, and 2 remain under treatment for their complications.

DISCUSSION

Acceptance of the concept of operative occlusion of the bronchus is facilitated when it is realized that auto-occlusion occurs in the natural course of cavitary tuberculosis. In 1940 we observed a left main bronchus that was pinpoint in size, and pus aspirated from it contained acid-fast bacilli. Five later bronchoscopic examinations failed to disclose an opening to the left main bronchus, and sputum cultures became negative. Chest films showed opacification of the left hemithorax. Auto-occlusion of a main bronchus had occurred.

An example of auto-lobar occlusion was provided in 1940 by a patient with a loud wheeze, positive sputum, and a pinpoint opening to the left upper lobe bronchus beneath an unsuccessful thoracoplasty. Stimulated by the work of Adams and Vorwald, the stenosed bronchial orifice was treated on three occasions with 35 per cent silver nitrate. Each time the wheeze disappeared and the sputum became negative, only to return 10 days later as the bronchus reopened. Eventually the bronchus closed permanently and, now, 20 years later, the wheeze is gone, the sputum is negative, and no cavity can be demonstrated. A similar lobar occlusion occurred in Case 2 of this report.

Auto-occlusion of a segmental bronchus was observed in a 49-year-old male who presented with infiltrative disease in the apical-posterior segment of the left upper lobe and with positive sputum. After 1 month of isoniazid and PAS, the sputum converted and remained negative. The residual disease focus was resected 8 months later and revealed fibrous closure of the segmental bronchus.

Ligation and division of the bronchus, as a surgical solution to cavity closure, is a technical adjunct designed to mimic the natural course of the disease. The procedure is old in principle, but its therapeutic realization was surprisingly slow to occur. To realize that auto-occlusion of the bronchus sometimes occurs in the natural course of cavitary disease was not enough. It was essential to learn that obstruction to drainage by bronchial occlusion was not harmful. We had to be assured that no secondary organisms were trapped in the cavity to set the stage for a fulminating lung abscess. Circulatory shunts, nutritional hazards with cavity rupture, bacteremia, and other potential hazards proved to be either nonexistent or avoidable surgically. Our errors were original errors, since we had no recourse to the mistakes of others.

The majority of authors reporting on the various aspects of collapse therapy focused their attentions on the technical maneuvers by which they achieved successful results. For example, the proponent of pneumcthorax might emphasize the size and frequency of refills; in extrapleural pneumothorax it was the degree of pressure; or if the surgeon had designed an improved type of thoracoplasty, he described in detail its technical merits. It is remarkable in retrospect how little attention was paid to the role of bronchial occlusion in the ultimate success of these varied collapse procedures. But now, we believe that surgical division of the bronchus should be recognized as a distinct surgical entity, not concealed beneath the therapeutic guise of thoracoplasty, pneumothorax, or other type of treatment, but to occupy its own definite place in the surgical treatment of cavitary tuberculosis.

This relatively new procedure, surgical division of the bronchus, is not to be compared with or substituted for pulmonary resection in the treatment of cavitary tuberculosis. In general, ligation and division of the bronchus begins where resection leaves off. That is to say, when the indications for resection have to be extended precariously, then bronchial division may prove to be a more acceptable solution.

In reviewing 300 cases of segmental resection,[63] it was noted that bronchial fistulas were most likely to occur when the upper lobe and the superior segment of the lower lobe were resected simultaneously. The fistulas were thought to be due to the difficulty in obliterating the residual pleural space. This observation was especially true on the left, when the lingula was resected along with the rest of the upper lobe. In such instances, to avoid a bronchopleural fistula, a preliminary thoracoplasty might be done so as to eliminate a space problem at the second stage when the resection is accomplished. In some cases the surgeon may elect to perform the thoracoplasty at the time of the resection, but the dimensions of such a combined operation are to be respected. Ligation and division of the proper bronchi, under these circumstances, offers an alternate solution for patients in whom the indications for resection are being extended beyond reasonable risk.

In an extensive report from England[64] on the surgical management of tuberculosis, it was concluded that there still is a significant place for the classical therapeutic thoracoplasty, if the hazards of extensive and complicated resections are to be avoided. This philosophy has great merit, but to it might be added that if the effectiveness of the thoracoplasty is to be ensured, then the procedure should be supplemented by the surgical division of the proper bronchi. The classical therapeutic thoracoplasty requires not only that long segments of ribs be removed, but that they must be removed in sufficient number to get well below the disease for an effective collapse. Such a procedure is deforming, it must be done in two or three stages, and it is costly to pulmonary function. The selective extraperiosteal thoracoplasty which is proposed at the time of bronchial division is not deforming, it can be done in one stage, and only short segments of ribs are stripped of their periosteum posteriorly. Therefore, function in the anterior chest is carefully preserved.

SUMMARY

1. Atelectasis exerts a favorable influence on pulmonary tuberculosis.
2. The key to successful cavity collapse is permanent occlusion of the draining bronchus or bronchi.
3. Auto-occlusion of the bronchus is an inconstant but fortunate event in the natural course of tuberculosis, and is in no way disturbing to the general physiology.
4. Ligation and division of the draining bronchus can mimic the beneficial effects of auto-occlusion and accomplish cavity closure and bacteriologic negativity.
5. A concept has been presented for the safe conduct of this operation, developed from experiences with 25 clinical cases.
6. Low morbidity and mortality rates will be accomplished if these basic concepts are followed.
7. Many patients unsuitable for resection or major collapse measures can be treated successfully by bronchial ligation and division.

REFERENCES

1. Mendelssohn, J. D.: Der Mechanismus der Respiration und Cirkulation, oder das explicirte Wesen der Lungenhyperamien, 2 p. 1, 384 pp., 11 Berlin, B-Behrs, 1845.
2. Lichtheim, L.: Versuche über Lungenatelektase, Arch. f. exper. Path. u. Pharmakol. 10: 54, 1879.
3. Elliott, T. R., and Dingley, L. A.: Massive Collapse of the Lungs Following Abdominal Operations, Lancet 1: 1305, 1914.
4. Pasteur, W.: The Bradshaw Lecture on Massive Collapse of the Lung, Lancet 2: 1351, 1908.
5. Pasteur, W.: Massive Collapse of the Lung, Brit. J. Surg. 1: 587, 1914.
6. Lee, W. E., Ravdin, I. S., Tucker, G., and Pendergrass, E. P.: Studies on Experimental Pulmonary Atelectasis, Ann. Surg. 88: 15, 1928.
7. Andrus, W. deW.: Observations on the Cardiorespiratory Physiology Following the Collapse of One Lung by Bronchial Ligation, Arch. Surg. 10: 506, 1925.
8. Gardner, L. U.: The Pathology of Artificial Pneumothorax in Pulmonary Tuberculosis, Am. Rev. Tuberc. 10: 501, 1925.
9. Van Allen, C. M., and Lindskog, G. E.: Obstructive Pulmonary Atelectasis, Arch. Surg. 21: 1195, 1930.
10. Baarsma, P. R., Dirken, M. N. J., and Huizinga, E.: Collateral Ventilation in Man, J. THORACIC SURG. 17: 252, 1948.
11. Van Allen, C. M.: Obstructive Pulmonary Emphysema and Collateral Respiration, Surg. Gynec. & Obst. 55: 303, 1932.
12. Adams, W. E., and Livingstone, H. M.: Obstructive Pulmonary Atelectasis, Arch. Surg. 23: 500, 1931.
13. Habliston, C. C.: Intrapleural Pressures in Massive Collapse of the Lung, Am. J. M. Sc. 176: 830, 1928.
14. Jacobaeus, H. C., and Westermark, N.: A Further Study of Massive Collapse of the Lung, Acta radiol. 11: 547, 1930.
15. Glenn, E. E.: Massive Atelectasis in Pulmonary Tuberculosis and Its Treatment by Artificial Pneumothorax, Am. Rev. Tuberc. 23: 507, 1931.
16. Packard, E. N.: Massive Collapse (Atelectasis) Associated With Pulmonary Tuberculosis and Tumor, Am. Rev. Tuberc. 18: 7, 1928.

17. Hennell, H.: Atelectasis as a Factor in the Evolution of Chronic Fibroid Tuberculosis, Am. Rev. Tuberc. 23: 46, 1931.
18. Korol, E.: Atelectasis in Pulmonary Tuberculosis, Am. Rev. Tuberc. 23: 493, 1931.
19. Zavod, W. A.: Tuberculous Dissemination During Therapeutic Pneumothorax, Am. Rev. Tuberc. 37: 5, 1938.
20. Coryllos, P. N., and Birnbaum, G. L.: Obstructive Massive Atelectasis of the Lung, Arch. Surg. 16: 501, 1928.
20a. Churchill, E. D.: Pulmonary Atelectasis With Especial Reference to Massive Collapse of the Lung, Arch. Surg. 11: 489, 1925.
21. Coryllos, P. N.: The Circulation in the Compressed Atelectatic and Pneumonic Lung, Arch. Surg. 19: 1346, 1929.
22. Coryllos, P. N.: Post-Operative Apneumatosis (Atelectasis) and Post-Operative Pneumonia, J. A. M. A. 43: 98, 1929.
23. Coryllos, P. N., and Birnbaum, G. L.: Alveolar Gas Exchanges and Atelectasis, Arch. Surg. 21: 1214, 1930.
24. Coryllos, P. N., and Ornstein, G. G.: Giant Tuberculous Cavities of the Lung, J. Thoracic Surg. 8: 10, 1938.
25. Eloesser, L.: Blocked Cavities in Pulmonary Tuberculosis, J. Thoracic Surg. 7: 1, 1937.
26. Poix, G., and Vincent, P. S.: Variations in Cavity Size and Occlusion of Draining Bronchus. Pathogenic Study, Rev. de la tuberc. 4: 1094, 1938.
27. Steele, J. D., Jr., Trevis, A. W., and Laboe, E. Q.: Unexpected Cavity Closure Following Re-Expansion of the Lung After Ineffectual Pneumothorax, J. Thoracic Surg. 7: 498, 1938.
28. Troisier and Chadourne: Collapse Therapy; Bronchial Obstruction in Relation to Cavity Drainage, Rev. de la tuberc. 5: 66, 1939.
29. Aufses, A. H.: Bronchial Obstruction and Collapse Therapy, Am. Rev. Tuberc. 42: 672, 1940.
30. Brunn, H., Shipman, S., Goldman, A., and Ackerman, L.: Tuberculous Cavitation and Transpleural Decompression, J. Thoracic Surg. 10: 485, 1941.
31. Coryllos, P. N.: How Do Rest and Collapse Treatment Cure Pulmonary Tuberculosis, J. A. M. A. 100: 480, 1933.
32. Coryllos, P. N.: The Mechanics and Biology of Tuberculous Cavities, Am. Rev. Tuberc. 33: 639, 1936.
33. Coryllos, P. N.: Importance of Atelectasis in Pulmonary Tuberculosis. Its Relation to Fibrosis and to the Pathogenesis and Healing of Tuberculous Cavities, Am. Rev. Tuberc. 28: 1, 1933.
34. Leriche, R., and Policard, A.: Physiologie pathologique, chirurgical, inflammations, effets des traumatismes, reparation des plaies, etc., Paris, 1930, Masson et Cie.
35. Adams, W. E., Van Allen, C. M., and Livingstone, H. M.: Bronchial Injury and Repair, Ann. Surg. 91: 342, 1930.
36. Adams, W. E.: Detailed Description of a Safe and Reliable Method for Closing Large Bronchi, J. Thoracic Surg. 3: 198, 1933.
37. Adams, W. E., and Vorwald, A. J.: The Treatment of Pulmonary Tuberculosis by Bronchial Occlusion, J. Thoracic Surg. 3: 633, 1934.
38. Escudero, L., and Adams, W. E.: Healing of Experimental Pulmonary Tuberculosis by Fascial Transplantation and Bronchial Ligation, Am. Rev. Tuberc. 38: 298, 1938.
39. Kawabata, A.: Experimental Investigations on the Influence of Atelectasis Upon Pulmonary Tuberculosis. II. Influence of Occlusion Atelectasis Upon the Development of Pulmonary Tuberculosis, Kekkaku 16: 28, 1938.
40. Adams, W. E.: Vascular Changes in Experimental Atelectasis: Morphological, Physiological and Biochemical, J. Thoracic Surg. 4: 377, 1934.
41. Adams, W. E., and Singer, J. J.: The Clinical Improvement of Pulmonary Tuberculosis by Massive Atelectasis, Am. Rev. Tuberc. 31: 373, 1935.
42. Davidson, L. R.: Discussion of paper by Eloesser, L., J. Thoracic Surg. 10: 501, 1940.
43. Coryllos, P. N.: The Surgery of Pulmonary Tuberculosis, Brooklyn, N. Y., 1937, Comet Press, Inc., p. 17.
44. Crafoord, C., and Frenckner, P.: A Case With Favorable Course of Bronchial Occlusion Produced by Means of Bronchoscopy as Complementary Operation After Thoracoplasty for Unilateral Pulmonary Tuberculosis, Acta otolaryng. 28: 187, 1940.
45. Melfi, J., Schverlich, M., and Tamborini, M.: Endobronchial Treatment of Tuberculous Cavities (in Spanish), Arch. argent. de tisiol. 30: 225, 1954.
46. Auerbach, O., Katz, H. L., and Small, M. J.: The Effect of Streptomycin Therapy on the Bronchocavitary Junction and Its Relation to Cavitary Healing, Am. Rev. Tuberc. 67: 173, 1953.
47. Auerbach, O.: Pulmonary Tuberculosis After the Prolonged Use of Chemotherapy, Am. Rev. Tuberc. 71: 165, 1955.

48. Thompson, J. R.: "Open Healing" of Tuberculous Cavities, Am. Rev. Tuberc. 72: 601, 1955.
49. Novy, F. G., and Soule, M. H.: Microbe Respiration. II. Respiration of the Tubercle Bacillus, J. Infect. Dis. 36: 168, 1925.
50. Loebel, R. O., Shorr, E., and Richardson, H. B.: The Respiratory Metabolism of the Tubercle Bacillus, 26th Meeting of the National Tuberculosis Association, 1930.
51. D'Esopo, N. D., Bernstein, S., Decker, A. M., Raleigh, J. W., and Steenken, W., Jr.: Bacteriology of Lesions Resected During Chemotherapy, Tr. 12th Conference on the Chemotherapy of Tuberculosis, Veterans Administration, Washington, D. C., February, 1953.
52. D'Esopo, N. D.: Current Status of Antimicrobial Agents in the Treatment of Pulmonary Tuberculosis, Am. J. Surg. 89: 617, 1955.
53. Dubos, R. J.: Notes From the Transactions of the 12th Veterans-Army-Navy Conference on Chemotherapy of Tuberculosis, Feb. 9-12, 1953, Am. Rev. Tuberc. 67: 874, 1953.
54. Björk, V. O., and Salen, E. F.: The Blood Flow Through Atelectatic Lung, J. THORACIC SURG. 20: 933, 1950.
55. Scott, H. W., Jr., Collins, H. A., Foster, J. H., and Avery, R. D.: Experimental Tuberculosis. V. Effects of Ligation of a Pulmonary Artery on the Pulmonary Lesions of Induced Bovine Tuberculosis in Rabbits, J. THORACIC SURG. 29: 518, 1955.
56. Iselin, M., et al.: Trait de Technique Chirurgicale, Paris, France, 1955, Masson et Cie, Tome IV, p. 233.
57. Quoted by Iselin,[56] p. 233.
58. Nissen, R., and Lezius, A.: Der Verschluss des Dranagebronchus als selbstotandiges oder erganzendes Behandlungsverfahren bei der kavernosen Lungentuberkulose, Deutsche med. Wchnschr. 13: 385, 1952.
59. Lezius, A.: Die Lungenresektionen, Stuttgart, 1953, Georg Thieme Verlag, p. 131.
60. Bogush, L. K., Gerasimov, N. I., and Savon, A. A.: Pereviaska Bronkhov V Lechenii Legochnogo Tuberkulesa (Bronchus Ligation in Treatment of Pulmonary Tuberculosis), Khirurgiia, Moskva 32 (8): 3-7, 1956.
61. Bogush, L. K.: Pereviaska Bronkhov Kak Noviji Sposob Lechenia Kavernosnogo Tuberkulesa (Bronchial Ligation as a New Method for Treatment of Tuberculosis With Cavitation), Sovetskaia Meditsina 21 (6): 45-50, 1957.
62. Margulis, M. S.: Primenenije Operacii Isorivonnoj Pereviaski Dolevogo Bronkha Pri Legochnom Kravotechenii Iz Tuberkulesnoj Kaverni (Isolated Ligation of a Bronchial Branch in Lung Hemorrhage From a Tuberculous Cavern), Khirurgiia, Moskova 33 (8): 90-91, 1957.
63. Chamberlain, J. M., Storey, C. F., Klopstock, R., and Daniels, C. F.: Segmental Resection for Pulmonary Tuberculosis, J. THORACIC SURG. 26: 471, 1953.
64. Chamberlain, J. M.: Discussion on Thoracic Surgery in Pulmonary Tuberculosis, Tr. NAPT Commonwealth Chest Conference: Chest and Heart Disease in the Commonwealth, London, 1958, Tavistock House North, p. 289.

DISCUSSION

DR. KENJI KAWAMURA, Kyoto, Japan.—Thanks for the privilege of the floor, Dr. Adams—also thanks to Dr. Chamberlain for the report of such fine results in the cases of ligation of the bronchus.

My comrade and my associate, Professor Kitagawa, also had 3 cases of bronchus ligation for tuberculous cavities 5 years ago, which were reported in Japan, but the results were not so good. Dr. Chamberlain's cases are all very good. It comes, perhaps, from nice selection of the locale of the ligation of the bronchus, I think.

Now I should like to speak about another operation for the same advanced, poor risk case of tuberculosis; that is, extrafacial bone chips packed with coagulated blood. I have used the rib transplantation on the pleura in 12 cases at first, and made sure of their healing process during 3 to 7 years after surgery. According to these observations, the operation was improved by the use of bone chips filled with coagulated blood. The effect of bone transplantation in the tissue near the tuberculous lung is based on experimental results which show calcium precipitation in tuberculous foci from bone calcium, and also from tooth. (Slide) This shows bone chips that were taken from a resected rib.

(Slide) Next you see bone chips mixed with homologous blood coagula; (slide) and then you see the operation, putting them into the extrapleural space after pulmonary collapse.

(Slide) This is a roentgenogram before operation of one of the cases (slide), and the next is 2 weeks after (slide), and then the next is after 3 months.

We have had 7 patients with such operations for advanced tuberculosis, and until now all of them have had good results. The longest case is 3 years, and the shortest case is one half a year.

DR. JOSEPH J. TIMMES, St. Albans, N. Y.—We have also had experience with division of the bronchus in the surgical treatment of cavitary tuberculosis in the past year and a half, and our results thus far parallel those of Dr. Chamberlain. In the recent past we have sectioned the right main-stem bronchus.

(Slide) This first slide represents a woman, 40 years of age, who has had many years of treatment for tuberculosis starting with a pneumothorax, and many attempts at medical therapy using various combinations of drugs. She came to us with a destroyed right lung, positive sputum, and the organisms resistant to the drugs. Her maximum breathing capacity was 24 liters per minute preoperatively.

We divided the bronchus and then closed each end with interrupted sutures, not using the ligation technique of Dr. Chamberlain. At the conclusion of the operation we did a tracheostomy, kept her on assisted ventilation for 48 hours, and her postoperative course was uncomplicated.

(Slide) Arterial studies done 2 months postoperatively show there is now no desaturation at rest, or after exercise. With 100 per cent oxygen the saturation increased to 100 per cent.

We can interpret these studies as indicating that the shunt which must be present, since the pulmonary artery and the veins are left intact, must be minimal, and I wonder if Dr. Chamberlain would comment about this phenomenon.

DR. WILLIAM M. TUTTLE, Detroit, Mich.—I am going to discuss this paper because I happened to be there when dogs' bronchi were being cauterized, and that goes back approximately 30 years.

Now, I do not believe that this is the right surgical approach to this problem. It did not work in the few clinical cases which I hope Dr. Adams will tell you about, although it did work in dogs. In 1 case shown here today I would have taken the lung out. In other words, more maneuvers are used to tie a bronchus or cut a bronchus and sew it on both sides than we use to take the lobe out. This, to me—I must speak frankly—is against all surgical principles. The principle of disease therapy is to cure the disease by medicine or by God or by surgery, [laughter] and I just can't go along with this. You leave the disease in and let the patient live with it, or you take it out, or you cure it by various medicaments.

DR. LAWRENCE M. SHEFTS, San Antonio, Texas.—I know that many in the audience have tried the very thing that Dr. Chamberlain has very ably presented here today, but I'd like to make one point: Dr. Chamberlain has not stopped doing resections, and neither will most surgeons here. This operation is fraught with dangers, and I think it should be left in the hands of the few who still want to continue with it until there is a larger series of cases to place it on a broader basis. But today there are very few patients to whom we cannot offer resectional surgery with a very respectable mortality and morbidity.

DR. CLARENCE CRAFOORD, Stockholm, Sweden.—The previous discussers have not, in my opinion, noticed that the type of material Dr. Chamberlain has presented is the type of material in which resection therapy would not be possible to carry through. There is a group of cases which are drug resistant, bilateral, and in which there is so much disease spread to other parts of the lungs that if resection were tried the patients would end up with empyemas and bronchial fistulas in practically every case. I think that in this limited small group, Dr. Chamberlain's suggestion is both sound and a very good one.

PRESIDENT ADAMS.—Since reference was made to our earlier work, I will merely make two remarks.

One is that the tubercle bacillus which we used would always lead to the death of the dogs, and it was very striking how relatively little or no tuberculosis developed in atelectatic lungs.

The second point is that the clinical cases selected—and there were only 4—all had huge cavities with secondary infection, and we were unable to occlude completely the bronchus in these cases.

When Dr. Chamberlain first spoke to me about his experience with obstruction of the bronchus by division and suture, I had the feeling that the results of obstruction should be similar in patients to those seen in animals. I would be very inclined to agree with Dr. Crafoord that the risk of resection would be very great in those cases in which the organisms were resistant to the drugs and the involvement was as great as he showed.

DR. CHAMBERLAIN (Closing).—I would like to thank all the discussers, especially Dr. Crafoord, and to point out to you the one point that Dr. Timmes did not make. I happen to know about his case. The patient technically was hopelessly nonresectable. It was impossible to remove the lung as it was described to me, and I am sure that his solution was the proper one.

Dr. Shefts made some excellent points. He pointed out that there are definite dangers to the ligation and division of the bronchus, and in the manuscript we have gone into great detail to point out the dangers.

I would like to close by adding a word of caution. I hope that you will not return to your respective environments and attack every therapeutic failure by ligating and dividing the bronchus. We have made many errors, and I hope that before you proceed with this operation you will take advantage of these mistakes by following certain basic principles of case selection and operative technique which we have formulated.

THE CULTURE OF TUBERCLE BACILLI FROM RESECTED SPECIMENS OF "NEGATIVE" PATIENTS

George J. Willauer, M.D., Charles Fineberg, M.D. (by invitation), Robert G. Johnson, M.D. (by invitation), and William P. Coghlan, M.D. (by invitation), Philadelphia, Pa.*

THE CLASSIC PAPER entitled "Simple Excision in the Treatment of Pulmonary Tuberculosis" by Ryan, Medlar, and Welles[1] was read by Dr. Ryan before the Thirty-first Annual meeting of this Association in Atlantic City in April of 1951. Since that presentation there has been a fundamental change in regard to the complete treatment of pulmonary tuberculosis. The principles of treatment no longer concern themselves with arrest but rather with excision of the residuals of the disease and possible bacteriologic cure.

A major area of disagreement about the indication for pulmonary resection in tuberculosis concerns itself with patients who have residual disease and negative sputum. Should these patients be subjected to resection or be continued on bed rest and antimicrobial therapy? D'Esopo and his associates[2] have stated that the relapse rate is no different in resected and unresected nodular residuals. Culture of resected specimens by this group revealed that most of the organisms were nonviable. Hobby and co-workers,[3] with special culture techniques, have demonstrated that tubercle bacilli present in closed necrotic lesions after long-term chemotherapy are not as "dead" as has been suggested by others.

Although investigators have identified tubercle bacilli in resected caseous nodules and cavities of patients with negative sputa, these organisms have been difficult to culture[4-9] (Table I). The reported incidence of live bacilli

TABLE I. PREVIOUS SERIES: SPUTUM-NEGATIVE PATIENTS

YEAR	INVESTIGATORS	NO. OF PATIENTS	TOTAL POSITIVE RESECTED SPECIMENS
1952	D'Esopo et al.[4]	84	15%
1955	Hobby et al.[5]	43	72%
1955	Adler et al.[6]	103	18%
1956	Stewart et al.[7]	47	23%
1956	Bell[8]	147	40%
1956	Wayne and Salkin[9]	201	15%
1957	Hurford and Valentine[10]	50	38%
1959	Nat. Jewish Hosp.[11]	113	5%
1960	Willauer	29	85%

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has varied from 5 to 72 per cent. Auerbach[12] has pointed out the danger of supposed negative lesions discharging viable tubercle bacilli into the tracheobronchial tree.

It was the purpose of this study to investigate the incidence of viable organisms in resected specimens from a series of patients with negative sputa.

Many investigators[13] have used elaborate techniques for the culture of tubercle bacilli from resected lung tissue. Some groups have kept the specimens at 4° C. for indefinite periods of time before taking material for culture. Others have used homogenizing procedures and digestion of material with sodium hydroxide or sulfuric acid. Hobby and her group washed the homogenate in bovine albumin in order to eradicate the "toxic" components of necrotic debris.

In contrast to these methods, we have utilized a simple and direct approach. Immediately following the surgical procedure, the surgeon examined the resected specimen utilizing sterile precautions. Areas of cavitation and nodularity were incised and the caseous material was transferred with a sterile loop directly to a culture tube slant. A heavy inoculum was used and the entire surface of the slant was streaked. The formula of the egg yolk medium which was used is given in Table II. The streaked slants were incubated at 37° C. They were read at weekly intervals and discarded at the end of 8 weeks.

TABLE II. EGG YOLK MEDIA

Fresh egg yolk	100 ml.
Distilled water	33 ml.
Sterile glycerine	3.2 ml.
2% sterile malachite green	1.3 ml.
Inspissated for one hour at 84° C.	

This study extended over a period of 6 years, 1952 to 1958. During this time 125 patients have had pulmonary resections. There were 89 lobectomies, 17 wedge resections, 11 segmentectomies, and 8 pneumonectomies. The patients were both private and ward. Because several physicians handled the medical care of these patients, their antimicrobial therapy was varied. The surgical

TABLE IIIA. BACTERIOLOGY OF PREOPERATIVE SPUTA AND RESECTED SPECIMENS

PATIENTS	SPUTUM	RESECTED SPECIMEN
91	+	+
25	−	+
5	+	−
4	−	−
125		

TABLE IIIB. DURATION OF NEGATIVE SPUTUM

MONTHS	NO. OF PATIENTS
0 to less than 3	9
3 to less than 6	3
6 to less than 9	10
9 to 12	3
	25

management was directed by one of us (G. J. W.). Of the 125 patients who were operated upon, 29 had negative sputa for periods of 1 to 12 months prior to resection (Table IIIA, IIIB). Twenty-five of the 29 patients with negative sputa proved to have viable tubercle bacilli in their resected specimens and form the basis of this report. The surgery performed on these patients consisted of 3 pneumonectomies, 10 lobectomies, 8 segmentectomies, and 4 wedge resections. The type of lesion found in relation to the surgical procedure performed is listed in Table IV. The involvement found at operation necessitating pneumonectomy in 3 patients cannot be regarded as residual disease. These 3 cases are included because the preoperative sputum was negative and the resected specimens grew tubercle bacilli.

TABLE IV. CORRELATION OF SURGERY AND PATHOLOGY

SURGICAL PROCEDURE	NO.	CAVITARY	NODULAR
Pneumonectomy	3	1	2
Lobectomy	10	8	2
Segmental resection	8	2	6
Wedge resection	4	1	3
Totals	25	12	13

Four patients had negative sputa prior to operation and culture of the resected specimens was negative. The remainder of the group, 96, had positive sputa at the time of resection. Resected lung tissue from 5 of these patients failed to grow tubercle bacilli.

The preoperative antimicrobial therapy was either continuous or interrupted. Included under continuous therapy were those patients who had pulmonary tuberculosis diagnosed on admission and who received continuous antimicrobial therapy to the time of resection. All others were classified as interrupted. In the 25 patients we are discussing, 15 had received continuous therapy and 10 had interrupted therapy. The shortest duration of continuous antimicrobial therapy was 4 months and the longest 27 months. The average was 11 months. These patients all received various combinations of streptomycin, isoniazid, and para-aminosalicylic acid. Fifteen patients were on two drugs; 10 patients were on three drug therapy. The majority of those on two drug therapy received streptomycin as one of the drugs.

Follow-up data were obtained on every patient in this group (Table V). This information was obtained from either the records of the Eagleville Dispensary or from the patient's physician. All patients in this series were discharged on antimicrobial therapy. The type and duration of antimicrobial therapy was thereafter controlled by the patient's physician. One patient died of pulmonary insufficiency following resection on the opposite side 1 year after the original operation. The only true failure of the group was in an uncooperative patient who showed evidence of activation in the lower lobe on the side of the resected lung and positive sputum 5 years following operation. The remaining 23 patients are well, sputa negative, and only 2 are still on antimicrobial therapy.

TABLE V. POSTRESECTIONAL FOLLOW-UP

NO. OF PATIENTS	YEARS AFTER RESECTION	SPUTUM	ANTIMICROBIAL THERAPY	RESULTS
1	8	−	No	Well
7	7	−	1	Well
4	6	1 + 3 −	1	3 well 1 spread of disease
1	5	−	No	Well
7	4	−	No	Well
2	3	−	No	Well
2	2	−	1	Well
1	1	1 +	1	Died 1 year later of pulmonary insufficiency
Total 25				

The very high percentage of viable tubercle bacilli obtained from resected specimens in this series is in contrast to other reported series. We believe that two important factors have led to this result: (1) the transfer of material was done immediately by the operating surgeon from the freshly resected lung tissue, and (2) the material was neither traumatized by maceration or by freezing techniques.

SUMMARY

1. In a series of 125 consecutive patients with pulmonary tuberculosis who had pulmonary resections, 29 had had negative sputa for a period of 1 to 12 months prior to resection.
2. Positive cultures for tubercle bacilli were obtained from the resected lung tissue in 25 of these 29 patients.
3. There were no operative deaths. One patient died a year later following a subsequent resection on the opposite side.
4. The patients have been followed from 1 to 8 years postoperatively. Twenty-three are clinically well. In all cases the sputa have remained negative.

CONCLUSIONS

1. Patients with negative sputum and residual lesions have viable tubercle bacilli in the resected specimens in a high percentage of cases.
2. Resectional surgery in this type of patient affords a better chance for permanent cure.

REFERENCES

1. Ryan, B. J., Medlar, E. M., and Welles, E. S.: Simple Excision in the Treatment of Pulmonary Tuberculosis, J. THORACIC SURG. 23: 327, 1952.
2. D'Esopo, N. D.: Current Status of Antimicrobial Agents in the Treatment of Pulmonary Tuberculosis, Am. J. Surg. 89: 617, 1955.
3. Hobby, G. L., Auerbach, O., Lenert, T. F., Small, M. J., and Comer, J. V.: The Late Emergence of M. Tuberculosis in Liquid Cultures of Pulmonary Lesions Resected From Humans, Am. Rev. Tuberc. 70: 191, 1954.
4. D'Esopo, N. D., Bernstein, S., Lee, W. F., Decker A. M., and Steenken, Wm. J.: The Bacteriology of Resected Lesions During Chemotherapy. Tr. Eleventh Conference on Chemotherapy for Tuberculosis: 230, 1952.

5. Hobby, G. L., Auerbach, O., Lenert, T. F., Small, M. J., and Vaughan, L. H.: The Recovery of Tubercle Bacilli From Resected Pulmonary Lesions. Tr. Fourteenth Conference on Chemotherapy of Tuberculosis: 180, 1955.
6 Adler, R. H., Mautz, F. A., Jr., Cline, J., and Morse, W. C.: A Study of the Viability of Tubercle Bacilli in Resected Pulmonary Tissue. Tr. Fourteenth Conference on Chemotherapy of Tuberculosis, Atlanta, Georgia 14: 172, 1955.
7. Stewart, S. M., Turnbull, F. W. A., and MacGregor, A. R.: The Influence of Chemotherapy on the Bacterial Content of Tuberculous Pulmonary Lesions. Tubercle 37: 388, 1956.
8. Bell, J. W.: The Problem of Resection Surgery for Pulmonary Tuberculosis in the Non-Infectious Patient With Persisting Cavitary Disease, Am. Rev. Tuberc. 74: 169, 1956.
9. Wayne, L. G., and Salkin, D.: The Bacteriology of Resected Tuberculosis Pulmonary Lesions. 1. The Effect of Interval Between Reversal of Infections and Subsequent Surgery, Am. Rev. Tuberc. 74: 376, 1956.
10 Hurford, J. V., and Valentine, W. H.: Viable Tubercle Bacilli in Closed Lesions, Tubercle 38: 194, 1957.
11. Heaton, A. D., Russel, W. F. J., Deust, J., and Middlebrook, G.: Combined Drug Treatment of Tuberculosis. IV. Bacteriologic Studies on the Sputum and Resected Pulmonary Lesions of Tuberculous Patients. J. Clin. Invest. 38: 1376, 1959.
12 Auerbach, O., Hobby, G., Small, M. J., Lenert, T. F., and Comer, J. V.: The Clinico pathologic Significance of the Demonstration of Viable Tubercle Bacilli in Resected Lesions, J. THORACIC SURG. 29: 109, 1955.
13. Hobby, G. L., Auerbach, O., Lenert, T. F., Small, M. J., and Comer, J.: The Viability of Tubercle Bacilli in Healed Tuberculosis Lesions Following Chemotherapy. Tr. Thirteenth Conference on Chemotherapy of Tuberculosis: 291, 1954.

DISCUSSION

DR PAUL C. SAMSON, Lafayette, Calif.—With the advent of chemotherapy there has developed a new classification in tuberculosis, the so called "open negative," and I would like to confine my remarks to the open-negative group rather than to the broader series of cases which were so ably presented by Dr. Coghlan.

The reason that I think it is important to keep hammering at this is that our medical confreres are feeling their oats a little these days, and a good many of them feel that if they once can get the sputum negative, that that is the answer to the problem, and we perhaps see less of these patients referred for surgery now than we did even a few years ago

Therefore, I think it's important to keep emphasizing the fact that with proper laboratory facilities and careful techniques, as you have just heard, many of these patients can be proved to contain viable bacilli, and, therefore, in my opinion, resection should be done.

Dr. Shebart and I reviewed a series of cases recently from the VAH Livermore. Our figures are similar to Dr. Coghlan's over a 2 year period. Thirty three cases in a group of 122 consecutive resections satisfied the requirement of "open negative," which means a cavity presumed or ascertained to be present from the x ray, and sputum negative for at least 3 months.

Of these 33, 23 (70 per cent) yielded positive cultures of the resected specimen

Now, it's interesting that several of the cultures of resected specimens were negative at the end of the 3 months. Three patients whose cultures of the resected specimens were positive had been negative to all clinical means for 12 months prior to surgery.

I think this paper is important because of some change in attitude on the part of our medical colleagues. Particularly in patients in the open negative group I believe resection should almost always be done.

DR. DAVID V. PECORA, Ray Brook, N. Y.—I think when we speak of the open negative group we should define our terms I do not believe that it represents a homogeneous group. This group discussed today is certainly not homogeneous, because it has included patients who had interrupted therapy, and also therapy of varying duration.

If we define the therapy carefully and also the duration, then we can obtain a somewhat different result.

We have not encountered a high relapse rate in patients treated with various combinations of streptomycin, PAS, and INH compounds, providing the organisms are susceptible and the therapy is continuous and prolonged. Although we attempt to remove cavitary disease whenever possible, we have not encountered a high relapse rate in those patients who, for one reason or another, have not had surgery, provided INH is one of the drugs employed.

Since January, 1950, we have made bacteriologic studies of 303 lesions resected from patients receiving various combinations of streptomycin, PAS, and INH continuously over prolonged periods. Our methods of culturing the organisms are similar to those presented.

Concentrated smears were positive for acid-fast bacilli in 66 per cent of the patients who had been sputum negative by culture for 6 months or less prior to surgery, and 64 per cent of those who had negative sputum for more than 6 months prior to surgery. On the other hand, cultures of resected pulmonary tissue were positive for tubercle bacilli in 9 per cent of the patients who had negative sputum cultures for 7 months or less prior to surgery. In no instance did we find a positive culture of tissue in a patient who had negative sputum cultures for over 7 months prior to surgery.

We have found no correlation between the incidence of postoperative tuberculosis complications or reactivations and the presence of nonculturable tubercle bacilli in the tissues. We have had no early tuberculous complications and less than 2 per cent late tuberculous complications in patients who have not harbored culturable tubercle bacilli in the resected tissues.

DR. LAWRENCE M. SHEFTS, San Antonio, Texas.—Very briefly, I agree emphatically with Dr. Coghlan's conclusions. In 20 to 25 per cent of our resected specimens in patients who have had a negative sputum for long periods of time, we were able to obtain organisms from the cavities. They are in the wall, thick and hard though it may be.

Many papers are being presented in today's literature on the follow-up of open negative cavities. When the internist figures a relapse rate of 5 per cent, and says that our relapse rate is the same from surgery, what is the point of operating? The point is that it is a difference in terminology between open negative cavities and open healed cavities.

COLON REPLACEMENT OF THE ESOPHAGUS IN CHILDREN FOR CONGENITAL AND ACQUIRED DISEASE

William E. Neville, M.D., and George H. A. Clowes, M.D.,
Cleveland, Ohio

INTRODUCTION

IN PREVIOUS REPORTS,[9, 11] we have presented our observations in patients operated upon for benign and malignant disease, in which segments of the colon have been used to reconstruct all or part of the esophagus and stomach. Among these the most gratifying results have been obtained in children with congenital esophageal defects and corrosive destruction.[2, 3, 5, 8] Heretofore, in these patients, the most successful reconstructions of an adequate swallowing mechanism have employed anterior, subcutaneous or retrosternal jejunal transplants.[4, 6, 7, 14]

The purpose of this paper is to present our operative technique and observations in children upon whom we have reconstructed the esophagus with the colon.

OPERATIVE TECHNIQUE

The operation is performed in one or two stages, depending upon the nature and extent of the disease.

Preoperative preparation consists of restoration of nutritional and chemical balance and sterilization of the colon. The latter is prepared for 2 to 4 days with neomycin (1 gram) every 6 hr. by mouth or through the gastrostomy tube, if this had been inserted for feeding purposes.

If the entire esophagus is to be reconstructed, the baby is operated upon in the supine position. If the child has had a previous esophagostomy, this is dissected from the surrounding tissue. The esophagus is exposed in the neck through an incision along the anterior border of the right sternocleidomastoid muscle (Fig. 1). The strap muscles are divided transversely over the thyroid gland. The esophagus is isolated posterior to the trachea just above the manubrium and dissected upward. The recurrent laryngeal nerve is identified and preserved.

Two operating teams have been employed. The abdomen is opened through a long upper midline incision from the xiphoid to below the umbilicus. The

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entire right colon is mobilized from the cecum to the hepatic flexure by incising its lateral avascular peritoneal attachments. The lesser peritoneal cavity is entered midway along the greater curvature and the gastrocolic omentum divided to the hepatic and splenic flexures. Thus, the entire colon is mobilized from the cecum to the splenic flexure. The ileocolic, right, and middle colic vessels are identified. To test the ability of the middle colic artery and vein to supplant the circulation of the colon, the right colic artery and vein are temporarily occluded with a bulldog clamp. In the interim the appendix and greater omentum are removed. If the circulation appears to be adequate, the right colic vessels are divided close to their origin. The proximal end of the bowel is transected at the ileocecal valve and the opening in the cecum is closed.

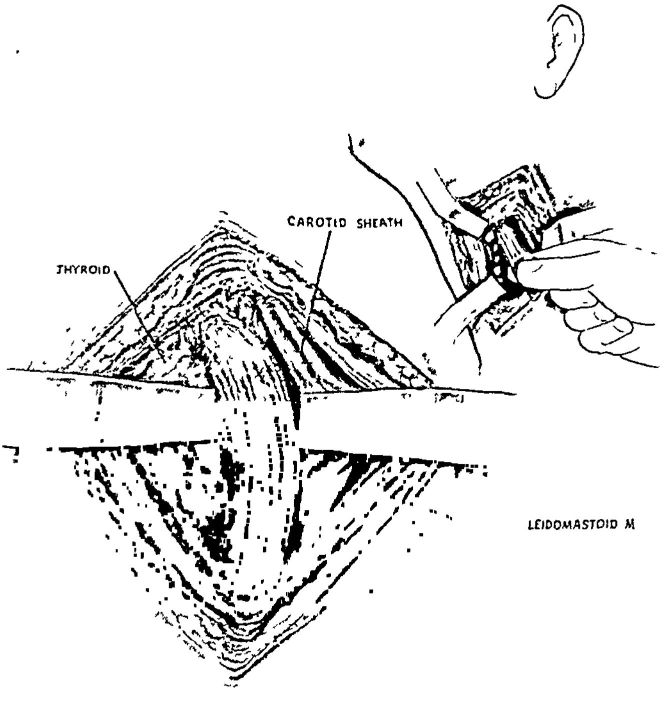

Fig. 1.—Exposure of the esophagus in the neck.

The right half of the colon is placed on the chest wall to determine its adequacy for esophageal reconstruction. If necessary, additional length can be obtained by further division of the mesentery on the right down to the origin of the vascular pedicle. A tunnel is created in the anterior mediastinum just posterior to the periosteum of the sternum from the xiphoid process to the manubrium by blunt dissection from below and above. The proximal end of the colon is passed into the neck, either in front of or behind the stomach, through this tunnel. The latter seems preferable because it offers additional length, and the duodenum is not compressed by the vascular pedicle. To widen the thoracic inlet it may be necessary to remove a V-shaped segment from the upper sternum. Having determined that the cecum will reach the neck without compromising its blood supply, the colon segment is isolated by dividing the transverse colon. Thus, the entire segment is suspended upon a vascular pedicle comprised of only the middle colic artery and vein (Fig. 2). The cervical esophageal colon anastomosis is performed, end-to-end, with two or three layers of interrupted fine silk. If the distal esophagus is not resected at this time, a catheter is inserted into this section and brought out through a stab wound to create a mucus fistula. Simultaneously, an opening is made on the anterior wall of the stomach and the distal end of the colon is anastomosed to this organ. Either a pyloromyotomy or a pyloroplasty may be performed. A tube gastrostomy, if not already present for preoperative feeding, is created to decompress the stomach in the early postoperative period. It may then be used for subsequent feedings until such time as the patient is able to eat normally. This maneuver obviates the necessity for an indwelling nasogastric tube. The continuity of the lower gastrointestinal tract is established with an end-to-end iliocolostomy.

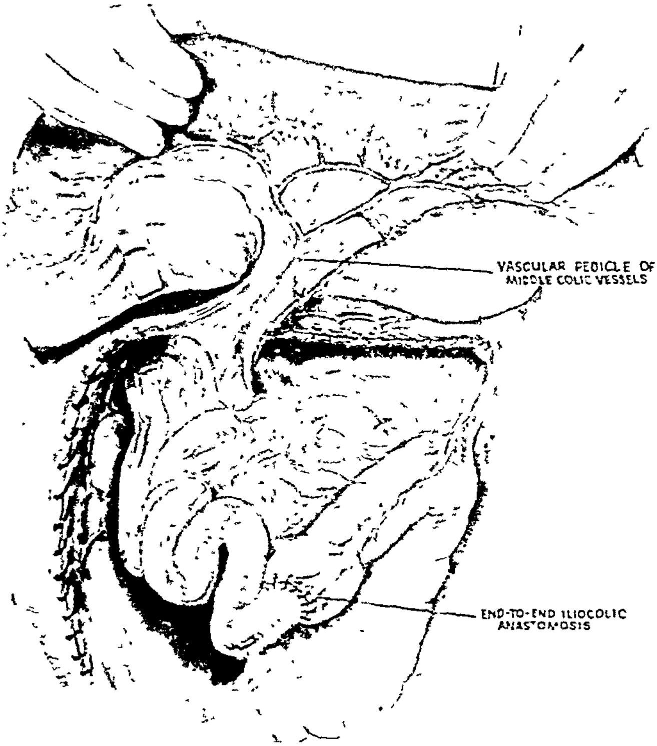
VASCULAR PEDICLE OF MIDDLE COLIC VESSELS
END-TO-END ILIOCOLIC ANASTOMOSIS

Fig 2.—Isolated colon segment suspended on a vascular pedicle of the middle colic artery and vein

Lesions within the thorax above the aortic arch are approached through a right thoracotomy and upper midline incision. The colon segment is delivered into the chest through an opening in the diaphragm anterior to the liver and placed along the anterior aspect of the right hilum.

Intrathoracic esophageal lesions below the aortic arch are approached through separate left abdominal and thoracic incisions. The diaphragm is transected from the hiatus outward. In this situation it is not necessary to mobilize the right colon. The transverse colon is usually of sufficient length to substitute for the resected esophagus. Following resection of the lesion, the proximal end of the bowel is passed into the left chest. The isoperistaltic esophagocolon anastomosis of the resected esophagus and the entire area are repleuralized. The opening in the cardia is closed and the distal end of the colon is anastomosed to the stomach anteriorly. A colocolostomy, pyloroplasty, and tube gastrostomy complete the operative procedure.

CASE REPORTS

CASE 1.—*Stricture of the lower esophagus following ingestion of corrosives.*

J. S., a 6-year-old boy, was admitted to University Hospitals on Oct. 19, 1953, shortly after swallowing muriatic acid. An emergency tracheotomy was performed because of difficulty in breathing. He was placed on cortisone and antibiotics. A barium swallow 1 week after admission demonstrated a stricture at the lower end of the esophagus and pyloric obstruction. Bougienage of the esophagus was successfully carried out but the pyloric obstruction persisted. Resection of the distal end of the stomach was performed on Dec. 10, 1953, a Billroth I type of procedure being performed. Despite repeated esophageal dilatations, dysphagia and vomiting persisted. Neuropsychiatric therapy was instituted because of absence of roentgenographic evidence of pyloric obstruction. Narrowing of the distal end of the esophagus was repeatedly evident by x-ray study and esophagoscopy. On several occasions it was necessary to remove a bolus of food from the esophagus. In June, 1955, x-ray studies of the esophagus and stomach showed 90 per cent gastric retention at the end of 6 hours. He was admitted to St. Alexis Hospital where revision of the gastroduodenostomy was done on July 1, 1955. The lower end of the esophagus was definitely narrowed, but there appeared to be normal passage of barium through this area. Following this, he was relieved of his symptoms only temporarily. On July 7, 1956, he was admitted to Cleveland Metropolitan General Hospital* for resection of the esophagus. Roentgenograms showed a persistent narrowing of the lower end of the esophagus with an adequate gastroduodenal stoma. On July 12, 1956, the lower end of the esophagus was resected and the transverse colon interpolated in an isoperistaltic manner between the esophagus and the stomach. His postoperative course was relatively uneventful. Tube feedings were begun on the seventh postoperative day and oral feedings on the tenth day. He was discharged on the sixteenth postoperative day at which time he was eating a normal diet. The gastrostomy tube was removed just prior to his leaving the hospital. Since then he has been completely asymptomatic. X-ray studies 1 year later at the Cleveland Clinic were normal. At the present time he can eat everything without discomfort or diarrhea. He weighs 58 pounds and is 56 inches tall.

CASE 2.—*Stricture of lower esophagus.*

R. M., a 5-year-old boy, was admitted to the hospital on June 20, 1957, complaining of difficulty in swallowing. His mother stated that he had swallowed lye 2 years previously. The subsequent stricture had been treated with frequent bougienage in another city. This was his first episode since the family had moved to Cleveland. X-ray studies of the esophagus showed narrowing at the lower end. On esophagoscopy, the scope could not be passed through the strictured segment. Dilatation was unsuccessfully attempted. He was operated upon on June 26, 1957. The left thorax was opened through the eighth interspace. The diaphragm

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*Formerly Cleveland City Hospital.

was incised from the hiatus to the costal margin. The lower end of the esophagus was resected from the level of the inferior pulmonary vein down to the stomach. The distal transverse colon was easily delivered into the chest after dividing the gastrocolic omentum and freeing the splenic flexure. The colon was divided proximally and distally and a pie-shaped segment with its attendant blood supply was interpolated between the cut end of the esophagus and the stomach. The colon was reunited and a gastrostomy completed the procedure. His postoperative convalescence was uneventful. The gastrostomy tube was removed before his discharge on the twenty-second postoperative day.

Postoperative symptoms of abdominal cramps and diarrhea occurred but disappeared within 8 weeks. Since that time he has been entirely asymptomatic.

CASE 3.—*Delayed reconstruction of esophagus in tracheoesophageal fistula with atresia.*

Baby F was operated upon July 22, 1954, at the age of 4 days, for a tracheoesophageal fistula with atresia. After ligation of the fistula, the lower end of the esophagus was resected. A feeding gastrostomy and cervical esophagostomy were performed.

On Aug. 22, 1955, an anterior mediastinal colon transplant was performed. With the baby in the supine position, the abdomen was opened through a long upper midline abdominal incision. The colon was mobilized from the cecum to the splenic flexure. It was transected proximally and distally after the existence of length adequate for esophageal reconstruction had been determined. The cervical esophagostomy was dissected free and a tunnel created in the anterior mediastinum just posterior to the periosteum of the sternum. The proximal end of the colon segment which was suspended on a pedicle of the middle colic artery and vein was passed through the mediastinal tunnel into the neck. An esophagocolostomy and cologastrostomy were performed concomitantly. A colocolostomy reunited the lower bowel.

His postoperative course was uneventful except for the development of a cervical fistula. This healed readily and he was eating normally at the time of his discharge. On Dec. 15, 1955, he was admitted to the hospital because of difficulty in swallowing. It was obvious that there was a stricture at the esophagocolostomy but, because of severe diarrhea and an elevated temperature, a revision of the anastomosis was postponed. On December 18, the infant suddenly became cyanotic and dyspneic which necessitated an emergency exploration of the neck. The dilated esophagus which was adherent to the skin was entered first. The colon was markedly narrowed at the thoracic inlet. The stricture was manually dilated with a clamp until an adequate opening was obtained. The esophagus was closed and a tracheostomy performed. The convalescence was uneventful.

In June of 1957, another episode of complete obstruction occurred. A bolus of food was removed from the cervical esophagus and the stricture again dilated. Subsequently, on 3 separate occasions, bougienage of the narrowed segment has been performed. In the past year and one half this has not been necessary. At the moment, the child eats everything without experiencing dysphagia. He is 46 inches in height and weighs 45 pounds.

CASE 4.—*Stricture of the entire esophagus.*

B. S., a 30-month-old Negro male child, was admitted to Cleveland Metropolitan General Hospital on Nov. 20, 1956, because of persistent regurgitation of 2 weeks' duration. No history of ingestion of corrosive material could be obtained from the mother. Barium swallow on Nov. 23, 1956, revealed two areas of narrowing of the esophagus, one at the midportion and the other 2 cm. proximal to the cardia. Esophagoscopy on Nov. 27, 1956, demonstrated narrowing of the lumen at 3 cm. The mucosa appeared reddened and friable. No attempt was made to pass the esophagoscope beyond this level, but a biopsy was obtained which subsequently proved to be chronic inflammatory tissue. Several hours following this procedure, the baby developed crepitation of the neck. A roentgenogram of the chest revealed subcutaneous emphysema and a pneumomediastinum. A superior mediastinotomy and a tube feeding gastrostomy was performed immediately. His recovery was uneventful except for aspiration on 120 c.c. of straw-colored fluid from the left hemithorax.

Progress x-ray studies showed persistent narrowing of almost the entire esophagus. Because of this, a two-stage operative procedure was considered, primarily to intercalate the colon between the normal esophagus in the neck and the stomach through a mediastinal tunnel without opening the chest, and subsequently to resect the remaining esophagus via a right thoracotomy.

He was operated upon on Jan. 30, 1957. With the child in the supine position the esophagus was exposed in the neck through an incision along the anterior border of the right sternocleidomastoid muscle. A V-shaped segment of the sternum was removed to increase the anterioposterior diameter at the thoracic inlet. This maneuver allows the colon to be displaced into the neck without constriction at this level. The esophagus was transected at the level of the manubrium and a small catheter inserted into the distal end in an attempt to create an external mucus fistula. This was brought out through a stab wound lateral to the original incision. Through a separate abdominal incision, the colon was mobilized in the usual manner. The cecal end was transplanted into the neck through a mediastinal tunnel and an end-to-end esophagocolostomy performed, 2 cm. below the inferior pharyngeal constrictor muscles. The distal end of the viable colonic segment was anastomosed to the stomach and a pyloroplasty was performed. An end-to-end ileocolostomy established lower intestinal continuity. His postoperative course was satisfactory. X-ray examination of the esophagus on March 26 demonstrated narrowing of the esophagocolostomy.

He was readmitted to the hospital on March 26, 1957, because of difficulty in swallowing. Oral ingestion of barium showed an area of narrowing at the level of the seventh cervical vertebra, with no delay in the passage of barium. Attempt at bougienage was unsuccessful and for this reason a revision of the anastomosis was undertaken. Following this, a fistula developed which closed in 12 days. He was admitted again on Aug. 5, 1957, with the same symptoms. A second revision of his esophagocolostomy was carried out, only this time the entire suture line was resected and a re-anastomosis performed with three layers of silk. Dilatations of this anastomosis were carried out at intervals to preclude the development of another stricture.

On June 30, 1958, through a right thoracotomy, the markedly cicatrized esophagus was resected from the cardiac junction to the thoracic outlet. His convalescence was entirely uneventful and he was discharged in good condition on July 12.

He was last seen in the Pediatric Out-Patient Department on April 27, 1959. His weight was 43½ pounds, a gain of 5 pounds in 6 months. The hemoglobin was 12.5 grams with total proteins of 6.4, with albumin of 4 and globulin of 2.5. He had no difficulty in swallowing.

CASE 5.—*Delayed reconstruction for esophageal atresia.*

Baby M was first seen July 1, 1957, at the age of 18 months. His mother stated that he had been operated upon in Germany at the age of 5 days because he could not swallow. Although the original operative record is not available, the fact that the child had a cervical esophagostomy and a feeding gastrostomy suggest that he had a tracheoesophageal fistula with atresia. From observation and physical examination, it was obvious that the baby had received excellent care. Except for the esophageal opening in his neck, a well-healed right thoracic incision, and a gastrostomy tube protruding from the left upper quadrant, no other abnormalities were detected. He weighed 22 pounds and his state of nutrition was good. A recent blood count showed a hemoglobin of 13 grams, hematocrit of 40, a serum protein level of 6.9, with an albumin of 4.2 and a globulin of 2.7. Since the parents were anxious that something be done to restore a swallowing mechanism as soon as possible and since examination disclosed no reason for delay, he was admitted to the hospital for operation on July 11.

With the child in the supine position, the abdomen was opened through an upper midline incision. The ascending and transverse colon were mobilized to the splenic flexure. The right colic artery was temporarily occluded to determine if the middle colic artery could ensure viability of the cecum. The bowel was transected first at the ileocecal junction, the opening in the colon closed, and the appendix removed. The right colic artery and vein were divided close to their origin when it was obvious after 10 minutes of occlusion that the marginal vessels could provide circulation to the ascending colon through the middle colic artery. The bowel was divided distally near the splenic flexure, thus leaving the segment of bowel suspended upon a vascular pedicle of the middle colic artery and vein. The cervical esophagostomy was dissected from the surrounding tissues and the cecal end of the colon transplanted into the neck through an anterior mediastinal tunnel. The esophagocolostomy was performed with fine interrupted silk and the cologastrostomy with continuous catgut. In this instance, the colon was brought up behind the stomach through the gastrohepatic omentum, as advocated by Haight. This maneuver not only adds length to the segment but it eliminates compression of the duodenum anteriorly by the tenuous middle colic pedicle. The abdomen and neck were closed in the usual manner.

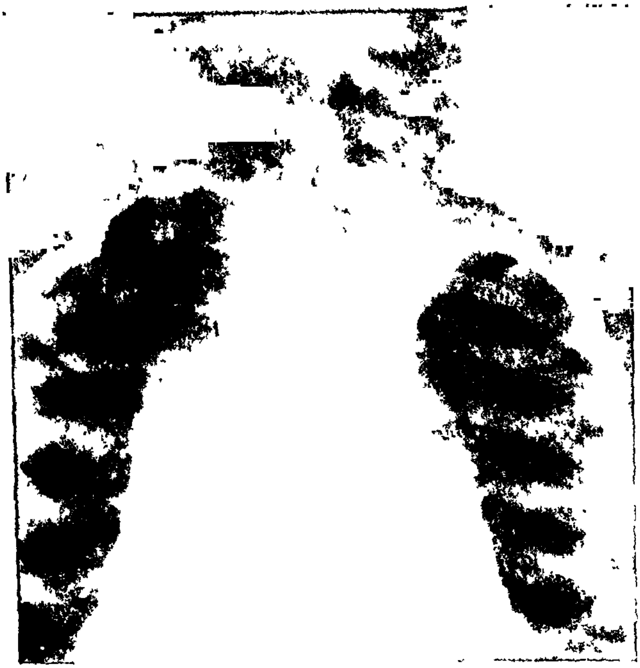

Fig. 3. Anterior mediastinal colon replacement of the esophagus 2 years following implantation. Although there is slight narrowing in the neck, no obstruction is present.

The child's postoperative course was entirely uneventful. Oral feedings were begun on the ninth day. It was a month, however, before he could swallow in a normal manner. The gastrostomy tube was removed when it became apparent that an adequate oral intake could be maintained.

He was readmitted to the hospital on Dec. 15, 1957, because of progressive dysphagia. A barium swallow demonstrated narrowing in the neck. Dilatation of this area was carried out the following day. On direct endoscopy, the stenosis appeared to be due to angulation at the esophagocolostomy near the thoracic inlet. A No. 33 metal dilator could easily be passed into the colon segment, making it appear that the difficulty in swallowing was due to malposition rather than cicatrization.

Since that time he has been in no real difficulty although an occasional brief episode of dysphagia has been experienced, relieved by a liquid diet for a few days.

A recent blood count disclosed a hemoglobin of 12 grams, red blood count of 4,000,000, with an hematocrit of 38. Total serum proteins were 6 grams, with an albumin of 3.5 and a globulin of 2.5. He is 37 inches tall and weighs 30 pounds. X-ray studies reveal slight narrowing of the lumen in the neck but no obstruction (Fig. 3).

RESULTS AND COMPLICATIONS

To date the colon has been used to reconstruct all or part of the esophagus and stomach in 46 patients for benign or malignant disease. Five of these patients are children who have been followed from 2 to 4 years following colonic implantation. As depicted in Table I, 3 infants had a colon transplant subsequent to corrosive destruction and 2 for esophageal atresia. All are alive and well at the present time.

TABLE I. RESULTS AND COMPLICATIONS

	LESION	OPERATIVE PROCEDURE	COMPLICATIONS	FOLLOW-UP (YEARS)
1.	Tracheoesophageal fistula with atresia	Anterior mediastinal colon transplant	Cervical fistula subsequent stenosis requiring revision and dilatation; no dilatation in the past 1½ years	4
2.	Tracheoesophageal fistula with atresia	Anterior mediastinal colon transplant	Angulation with stenosis which responded to dilatation	2
3.	Corrosive destruction of entire esophagus	Anterior mediastinal colon transplant	Cervical fistula; stenosis requiring revision and dilatation; no dilatation in past 6 months	2½
4.	Corrosive destruction of the lower esophagus	Resection of lower esophagus; intrathoracic replacement with the transverse colon	Abdominal cramps and diarrhea which abated within 2 months	3
5.	Corrosive destruction of the lower esophagus	Resection of lower esophagus; intrathoracic replacement with the transverse colon	Early abdominal cramps and diarrhea	2

In the 2 children in whom the colon was transposed into the neck through an anterior mediastinal tunnel, an anastomotic leak occurred. A subsequent stricture ultimately developed which necessitated revision and dilatation. This is comparable with our experience for high esophageal anastomosis in patients operated upon for carcinoma. In those patients in whom a cervical fistula developed in the early postoperative period, even though this healed readily, a stricture ensued which necessitated either revision or dilatation.

In colonic substitution of the lower esophagus, the complications have been of relatively short duration and have required no further operations. Diarrhea and abdominal cramps have been an early complaint. In 1 boy these persisted for nearly 6 months. During the interim, he was investigated thoroughly at another clinic with negative results. The symptoms are related to the ingestion of food and appear to be some type of gastrocolic reflex. This same symptom complex has been observed in patients following esophagogastrectomy for carcinoma.

DISCUSSION

Although the majority of the colon transplants have been performed in our patients for carcinoma,[1, 7, 15-17] with satisfactory palliation, the operation per se has far wider applicability in children and adults for benign conditions which impair passage of food through the esophagus. The problem of reconstituting an adequate permanent swallowing mechanism in infants with congenital atresia or chemical cicatricial fibrosis has concerned many surgeons.

The colon has many advantages over the stomach and the jejunum. The blood supply is excellent. Due to the anatomic distribution of the marginal arteries, a segment of viable bowel can be mobilized from the cecum to the descending colon if the middle colic artery and vein are left intact. The mucosa is resistant to acid peptic digestion as attested clinically by esophagoscopy and postmortem microscopic examination in patients dying of disease up to 30 months following implantation.[10] Experimentally, the colon transplants in dogs sacrificed up to 9 months showed no evidence of ulceration even though regurgitation was common because of the horizontal position of the animal.[9]

We have been particularly impressed by its length in babies and children. This is due to the redundancy of the transverse colon and the presence of a thin pliable mesentery. Thus, it is an ideal esophageal substitute in congenital atresia or corrosive strictures when long segments are involved.

Although revision and dilatation of the strictured cervical anatomosis was necessary in the 3 children who had an anterior mediastinal colon transplant, they can eat in a normal manner at the present time. It is apparent that, when a cervical fistula develops, the resultant cicatrix will invariably narrow the esophagus sufficiently to cause difficulty in swallowing. When this occurs, an early excision of the suture line with a secondary end-to-end anastomosis is recommended. Angulation of the esophagocolon segment in the neck can be prevented by having the colon lie in a redundant position. In this manner the pharyngoesophagus will not be stretched in a posteroanterior direction around the trachea.

Our original concern over the ability of this colon segment and accompanying vessels to lengthen with the growth of the child has been dispelled. Frequent x-ray examination has demonstrated that the substitute esophagus elongates, commensurate with the growth of the child. Fluoroscopically, regular contractions are evident which propel the bolus along the transplanted colon to the stomach. This, together with a normally placed stomach below the diaphragm, accounts for the excellent nutrition of the infants. None of the patients with high esophagocolostomies exhibits any evidence of colitis or gastritis. The infants in whom the lower esophagus was replaced with the colon have no regurgitation and esophagitis is completely absent. In addition to frequent x-ray evaluation of the esophageal substitute, their general nutritional status is catalogued by weight gain and blood counts. Except for 1 child, who experienced some gastrointestinal difficulty for 6 months, the weight gain in all patients has been progressive. Hemoglobin, red blood count and serum proteins have all been within normal limits.

SUMMARY

1. The technique for reconstruction of the esophagus in infants with corrosive destruction and congenital atresia is described.

2. The results and complications in 5 children closely followed from 2 to 4 years are presented.

3. The rationale of using the colon in preference to the jejunum or stomach is presented, combined with our experience in 46 patients operated upon for malignant and benign disease.

4. The fact that these children are growing in a normal manner and have no apparent difficulties attest to the fact that the colon can serve as the esophagus both entirely or in part.

REFERENCES

1. Battersby, S.: Paper presented at Society of University Surgeons, Indianapolis, Ind., February, 1956.
2. Dale, W. A., and Sherman, C. D., Jr.: Late Reconstruction of Congenital Esophageal Atresia by Intrathoracic Colon Transplantation, J. THORACIC SURG. 29: 344, 1955.
3. Haight, C.: Some Observations on Esophageal Atresia and Tracheoesophageal Fistula of Congenital Origin, J. THORACIC SURG. 34: 141, 1957.
4. Harrison, A. W.: Transthoracic Small Bowel Substitution in High Stricture of the Esophagus, J. THORACIC SURG. 18: 316, 1949.
5. Koop, C. E., and Raddy, S. R.: Colonic Replacement of Distal Esophagus and Proximal Stomach in the Management of Bleeding Varices in Children, Ann. Surg. 147: 17, 1958.
6. Longmire, W. P., Jr., and Ravitch, M. M.: A New Method of Constructing an Artificial Esophagus, Ann. Surg. 123: 819, 1946.
7. Mahoney, E. B., and Sherman, C. D., Jr.: Total Esophagoplasty Using Intrathoracic Right Colon, Surgery 35: 937, 1954.
8. Neville, Wm. E., Smith, A. E., and Storer, J.: Use of the Transverse Colon for Reconstruction of the Esophagus in Tracheo-Esophageal Fistula, Ann. Surg. 144: 1045, 1956.
9. Neville, Wm. E., and Clowes, G. H. A., Jr.: Reconstruction of the Esophagus With Segments of the Colon, J. THORACIC SURG. 35: 2, 1958.
10. Neville, Wm. E., and Clowes, G. H. A., Jr.: Reconstruction of Upper Gastrointestinal Tract With Colon Segments After Esophagogastrectomy, A. M. A. Arch. Surg. 77: 376, 1958.
11. Neville, Wm. E., and Clowes, G. H. A., Jr.: Reconstruction of the Esophagus and Stomach With Segments of the Colon, A. M. A. Arch. Surg. 77: 816, 1958.
12. Patterson, R. H., and Robbins, S. G.: Substitution Right Colon for the Esophagus, Ann. Surg. 147: 854, 1958.
13. Petrov, B. A.: Retrosternal Artificial Esophagus From Jejunum and Colon, Surgery 45: 890, 1959.
14. Robertson, R., and Sarjeant, T. R.: Reconstruction of the Esophagus, J. THORACIC SURG. 20: 689, 1950.
15. Scanlon, E. F., Morton, D. R., Walker, J. M., and Watson, W. L.: The "Case" Against Segmental Resection for Esophageal Carcinoma, Surg. Gynec. & Obst. 101: 290, 1955.
16. Sherman, C. D., Jr., Mahoney, E. B., Dale, W. A., and Stabins, S. J.: Intrathoracic Transplantation of Right Colon for Esophageal Reconstruction, Cancer 8: 1198, 1955.
17. Watson, W. L., and Cliffton, E. C.: Total Esophagoplasty Using Right Colon, Cancer 10: 488, 1957.

COARCTATION OF THE ABDOMINAL AORTA

Åke Senning, M.D., and Lennart Johansson, M.D., Stockholm, Sweden

After the first successful operation for coarctation of the aorta by Crafoord in 1945, aortic surgery has advanced at a tremendous rate. In addition to the usual localization in the isthmus of the aorta, a coarctation may be present at any site along the whole course of the vessel. Coarctation of the abdominal aorta is of particular interest, in view of its relation to the celiac, mesenteric, and renal arteries. Altogether 29 such cases have been described earlier.[1-27, 29-31] The coarctation consists either of a stricture involving a segment of varying length, or of hypoplasia of the distal part of the aorta. In 6 of the cases reported in the literature, the aorta was hypoplastic. The stenosis started suprarenally or at the level of the renal arteries in 16 patients, and was situated infrarenally in 11.

The pathogenesis of coarctation of the abdominal aorta is unknown. In a case described by Glenn and his associates,[12] Recklinghausen's disease was present, and caused strangulation of the aorta by neurofibromatous tissue, a situation similar to that found in 1 of our patients.

In the cases reported, the incidence seems to have been the same in both sexes. In 10 patients who died of the disease, the average age was 34 years. Coarctation of the abdominal aorta thus seems to be as serious as coarctation in the isthmus.

Clinically, infrarenal coarctation is characterized by signs of arterial insufficiency, with intermittent claudication, accompanied by moderate hypertension. Suprarenal coarctation produces the same clinical features as those of coarctation of the isthmus, that is, marked hypertension in the upper part of the body, headache, dizziness, and precordial pain. The femoral artery pulse is faint or impalpable. Signs of overloading of the left side of the heart are found, and there is a systolic pressure gradient between the aorta above and below the stenosis. Signs of an increased collateral circulation are sometimes present. A systolic murmur is often audible in the abdomen over the stenosed area. No clinical signs of an impaired blood flow through other organs than the kidneys—for example, the liver, pancreas or intestines—have been described. A definite diagnosis is established by aortography, with injection of contrast medium into the aorta proximal to the stenosis.

Few accounts of surgical treatment of coarctation of the abdominal aorta are found in the literature. Sympathectomy was undertaken in 4 cases, with

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no appreciable effect.[3, 12, 18, 25] In 3 patients with signs of unilateral renal damage, nephrectomy was performed. One patient died, and the condition of the others remained unchanged.[3, 7, 8]

When the renal arteries were not involved in the stenosis, a bypass operation has been performed. Glenn and his colleagues[12] used the splenic artery, after splenectomy, for bypass of a short stenosis directly proximal to the celiac artery. Beattie[5] and Gerbasi[11] and their co-workers performed aorto aortic bypass with insertion of an homologous vessel graft.

Resection of a membranous stricture between the celiac artery and the renal arteries, with good results, was reported by Gustavino and Becu.[15] Albanese and Baila[2] *performed infrarenal resection of the aorta but the patient* died postoperatively of anuria.

An account of 3 cases of coarctation of the abdominal aorta in which operation was performed follows

CASE REPORTS

Case 1.—The patient was a 12 year old girl who had had dizziness, headache, and hypertension in the upper part of the body since 10 years of age. The femoral artery pulse was impalpable on either side. The heart was enlarged, with left ventricular hypertrophy. Aortography showed a 6 cm. long coarctation of the abdominal aorta, involving the region of the celiac and superior mesenteric artery and both renal arteries. Distal to the coarctation, the aorta was of normal width.

Operation was performed in May, 1957, under hypothermia (28° C.).[16] A thoraco abdominal incision was made at the level of the eighth thoracic vertebra, and the aorta was dissected out retroperitoneally. The stenosed, fibrotically hard, aortic wall was surrounded by abundant periadventitial tissue. This tissue was removed from around the aorta and the origin of the large vessels, and the latter became strongly dilated At the origin of the renal arteries, their diameter—which was 3 to 5 mm before operation—was increased to 6 to 8 mm. after dissection. The aorta was split lengthwise for 8 cm from slightly above the stenosis to slightly below it A strip graft,[28] pointed at both ends, of freeze dried homologous vessel material was sutured into this incision. In view of the patient's age and expected growth, the prosthesis was made 30 per cent larger than the current requirement Postoperative aortography showed that the diameter of the stenosed segment had increased from 4 to 5 mm. to 20 mm. and that the vessels given off from it were of normal width (Fig. 1).

Operation produced a fall in blood pressure in the upper part of the body from 200/130 to 135/100 mm. Hg, and a rise in the lower part of the body from 125/? to 170/110 mm Hg. Both femoral artery pulses were distinctly palpable. The heart volume was decreased Renal function, evaluated by creatinine, para-aminohippurate and inulin clearance was normal, as before operation. At the time of writing (1½ years after operation) the patient is asymptomatic

Case 2.—A 25 year-old man with Recklinghausen's disease was found, at 14 years of age, to have arterial hypertension at a routine examination. He had no cardiovascular symptoms. He had the same type of coarctation of the abdominal aorta as the preceding patient, and was operated upon in the same way. A knitted Dacron prosthesis was used as a graft In this case, the aorta and the origin of the large vessels given off from it were surrounded by abundant, highly differentiated ganglioneuronic tissue. Infrarenally, the aorta appeared somewhat hypoplastic.

The arterial blood pressure in the upper part of the body, which was 180 210/120 mm. Hg before operation, fell to 150/80 mm. Hg after it. However, as can be seen in the

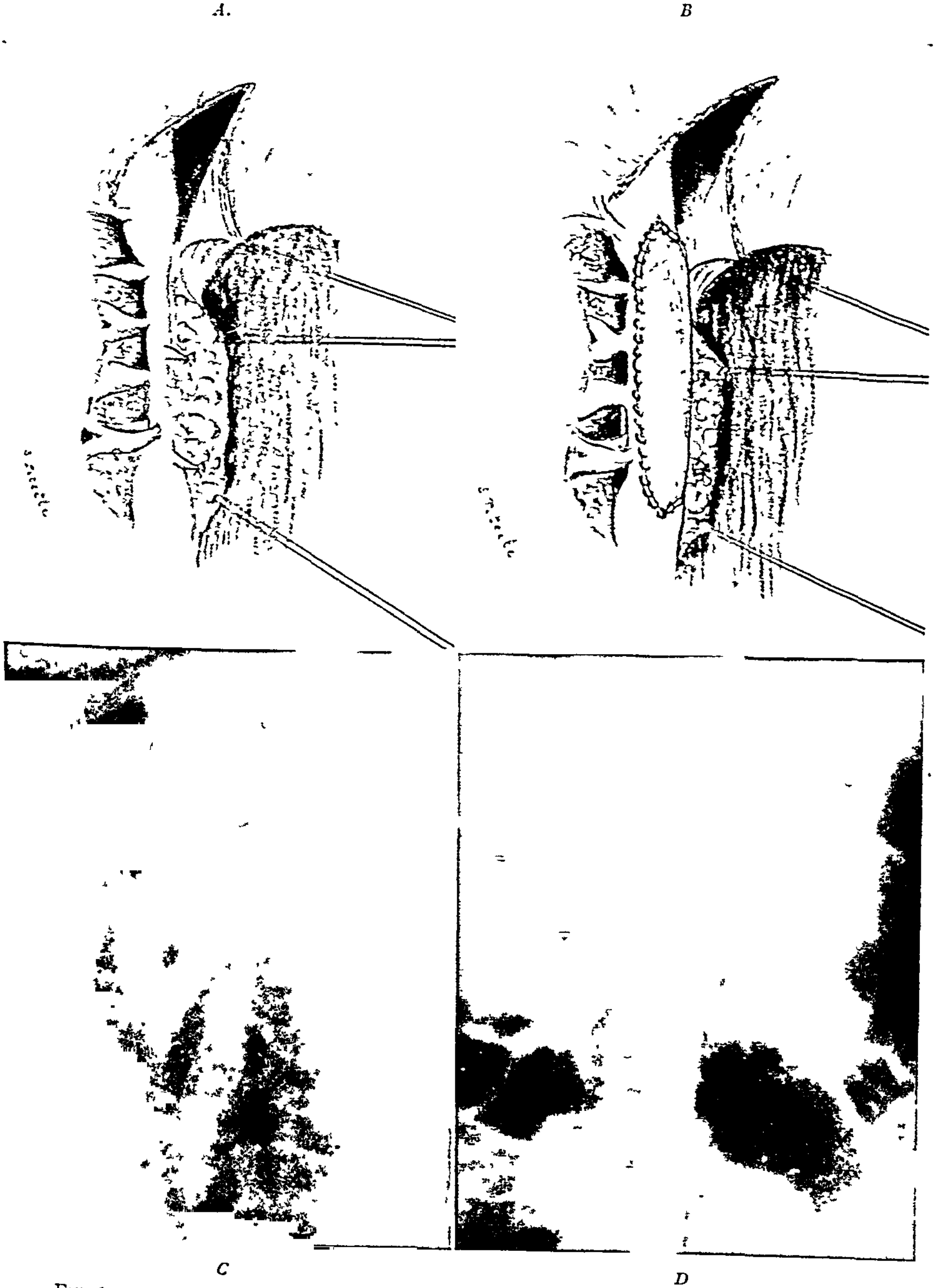

Fig 1.—*A*, Drawing showing coarctation of the abdominal aorta after retroperitoneal mobilization

B, After removal of periadventitial tissue and insertion of a strip-graft in the posterior aortic wall

C, Preoperative aortography

D, Postoperative aortography The vessels involved in the stenosis are, from below, the renal arteries, the superior mesenteric and the celiac arteries

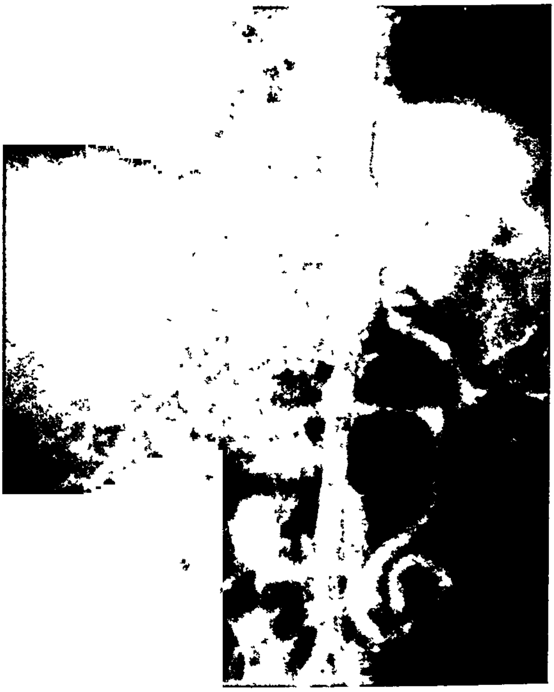

Fig. 2.—Case 2. Postoperative aortography. There is partial stenosis of the left renal artery 2 cm. from its insertion in the aorta, as well as 2 aneurysms of the right renal artery. The aorta is somewhat hypoplastic distal to the coarctation.

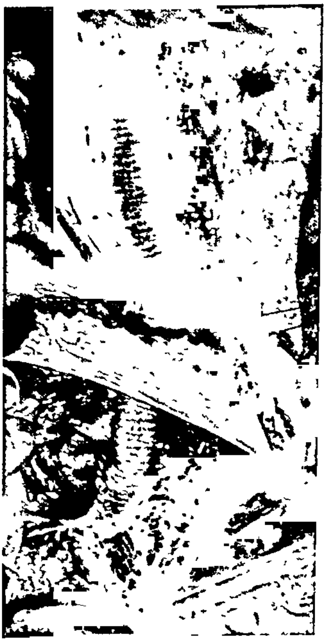

Fig. 3.—Thoraco-abdominal, aorto-aortic bypass from 10 cm. above the diaphragm. Dacron graft is sutured distally into an incision in the posterior aortic wall, extending from above the superior mesenteric artery to below the renal arteries.

postoperative aortogram (Fig. 2), a stricture was present in one renal artery, and two aneurysms in the other. Moreover, owing to hypoplasia of the aorta, a systolic pressure gradient of 25 mm. Hg between the thoracic aorta and the femoral artery was still present after operation. The para-aminohippurate and inulin clearance were the same pre- and postoperatively, and renal function was normal in other respects. The patient is asymptomatic and fully fit for work.

Case 3.—The patient was a 40-year-old woman with arterial hypertension (280/140 mm. Hg). Both femoral artery pulses were faint. Aortography showed coarctation at the level of the diaphragm and slightly above it. Distal to the stenosis, the aorta was occluded by calcium deposits beyond the level of the renal arteries. Infrarenally, the aorta was hypoplastic. Operation consisted of an aorto-aortic bypass with a Dacron graft. The aortic wall proximal to the stenosis was arteriosclerotic and friable. A knitted Dacron prosthesis was sutured end-to-side into the aorta, 10 cm. above the diaphragm. The aorta was split lengthwise at the level of the renal arteries, up to beyond the superior mesenteric artery. The calcium deposits in the aorta were removed, to allow free passage to the renal and superior mesenteric arteries and relatively good passage to the celiac artery. When the Dacron graft, with its distal end cut obliquely, was sutured end-to-side into the aortic incision, the aorta became widened locally (Fig. 3).

Operation produced a fall in blood pressure from 280/140 to 135-175/110 mm. Hg. The femoral artery pulses were stronger. Renal function was normal both before and after operation.

DISCUSSION

Coarctation of the abdominal aorta is a relatively rare disease; only 25 cases have, in fact, been reported during the past 10 years. The prognosis seems to be comparable to that in coarctation of the aortic isthmus, and the indications for operation seem to be the same. The diagnosis is established by aortography, with injection of contrast medium into the descending aorta above the stenosis.

In those cases in which the renal arteries are not involved in the coarctation, surgical treatment presents no great problems. Organs supplied with blood from the large vessels given off from the abdominal aorta other than the kidneys manage by means of collaterals only, with no clinical signs of hypoxia. In such cases, a simple bypass operation can be performed. This has been done earlier, with successful results, in 5 cases reported in the literature. In 1 case, resection could be performed.

When, on the other hand, the renal arteries are involved, the primary aim is to ensure a good blood supply to them. In (the present) Cases 1 and 2, dilatation of the renal arteries, at their origin from the stenosed aorta, was achieved by freeing them from periadventitial and adventitial tissue. The coarctation was then widened by splitting the aorta lengthwise, and inserting a strip-graft from behind.

In Case 3, the renal arteries were given off from the slightly hypoplastic aorta distal to the coarctation, and intra-aortic calcifications, which impeded passage of blood to the renal arteries among other vessels, were also present distal to the coarctation. An aorto-aortic bypass with a graft was therefore performed. The distal end of the graft was cut very obliquely and sutured into a longitudinal incision in the aorta, extending from above the superior mesenteric artery to distal to the renal arteries (see Fig. 3). When calcified material inside the aorta at the level of the renal arteries and superior mesenteric artery had been removed, the distal end of the graft was sewn into the incision. This resulted in local widening of the aorta, and ensured good passage of blood to the renal arteries.

The blood pressure fell postoperatively in all 3 patients; in Cases 1 and 3 it fell appreciably, whereas the fall was fairly moderate in Case 2. This patient still has a stricture of one renal artery, and two aneurysms of the other.

It has not been possible to establish whether a special renal factor exists, which influences the rise in blood pressure. Renal function was normal both pre- and postoperatively in all 3 cases, and no significant difference in renal blood flow took place.

Since all 3 patients are subjectively healthy postoperatively, it appears that operation is to be recommended. In most cases of coarctation of the abdominal aorta, a bypass operation, performed as in Case 3, would presumably improve the patient's condition, even if the aorta is hypoplastic distal to the renal arteries. In those cases in which the coarctation involves the region from above the celiac artery to just distal to the renal arteries, the strip-graft technique seems to be the method of choice. It relieves the stenosis, and increases the blood flow to the kidneys, as well as to the pancreas, spleen, and other organs.

SUMMARY

An account is given of 3 patients with coarctation of the abdominal aorta operated upon through a thoraco-abdominal incision, and retroperitoneal mobilization of the aorta. In 2 cases a strip-graft technique was used, and, in the third case, aorto-aortic bypass was performed. The results were good in all 3 cases.

REFERENCES

1. D'Abreu, A. L., Rob, C. G., and Vollmar, J. F.: Die Coarctatio Aortae abdominalis, Langenbecks Arch. klin. Chir. 290: 521, 1959.
2. Albanese, A. R., and Baila, M. R.: Congenital Coarctation of Abdominal Aorta, Bol. y trab. Acad. argent. cir. 37: 211, 1953.
3. Bahnson, H. T., Cooley, R. N., and Sloan, R. D.: Coarctation of the Aorta at Unusual Sites. Report of Two Cases With Angiocardiographic and Operative Findings, Am. Heart J. 38: 905, 1949.
4. Baylin, G. J.: Collateral Circulation Following Obstruction of Abdominal Aorta, Anat. Rec. 75: 405, 1939.
5. Beattie, E. J., Jr., Cooke, F. N., Paul, J. S., and Orbison, J. A.: Coarctation of the Aorta at the Level of the Diaphragm Treated Successfully With a Preserved Human Blood Vessel Graft, J. Thoracic Surg. 21: 506, 1951.
6. Bunnag, T. S.: Coarctation of the Abdominal Aorta at the Origin of the Inferior Mesenteric Artery, Am. J. Roentgenol. 78: 1003, 1957.
7. Doumer, E., Lorriaux, A., and Steenhauwer, B.: Hypertension artérielle paraplasie de l'artère rénale gauche avec malformation de l'aorte abdominale. Action passagère de la néphrectomie, Arch. mal. coeur 44: 446, 1951.
8. Fisher, E. R., and Corcoran, A. C.: Congenital Coarctation of the Abdominal Aorta With Resultant Renal Hypertension, Arch. Int. Med. 89: 943, 1952.
9. Freeman, N. E., Miller, E. R., Stephens, B., and Olney, M. B.: Retrograde Arteriography in the Diagnosis of Cardiovascular Lesions. II. Coarctation of the Aorta, Ann. Int. Med. 32: 827, 1950.

10. Froment, R., Gallavardin, L., and Noel, G.: Des formes basses, sous-isthmiques, de sténoses congenitales de l'aorte à propos de trois cas personnels, Arch. mal. coeur 45: 496, 1952.
11. Gerbasi, F. S., Kibler, R. S., and Margileth, A. M.: Coarctation of the Abdominal Aorta. A Case Successfully Treated Surgically, J. Pediat. 52: 191, 1958.
12. Glenn, F., Keefer, E. B. C., Speer, D. D., and Dotter, C. T.: Coarctation of the Lower Thoracic and Abdominal Aorta Immediately Proximal to the Coeliac Axis, Surg., Gynec. & Obst. 94: 561, 1952.
13. Gliedman, M. L., Ayers, W. B., and Vestal, B. L.: Aneurysm of the Abdominal Aorta and Its Branches. A Study of Untreated Patients, Ann. Surg. 146: 207, 1957.
14. Goldzieher, J. W., McMahon, H. E., and Goldzieher, M. A.: Coarctation of Abdominal Aorta Simulating Pheochromocytoma, A. M. A. Arch. Int. Med. 88: 835, 1951.
15. Guastavino, G. N., and Becu, L.: Coarctaciones aórticas ubicadas por debajo del sitio habitual (un caso operado de doble coarctación). Resección y homoinjerto, Rev. Asoc. méd. argent. 7: 347, 1956.
16. Hansson, J., Ikkos, D., Johansson, L., Rudhe, U., and Senning, Å.: Coarctation of the Abdominal Aorta. Case Report and Description of Successful Surgical Treatment, Acta chir. scandinav., Suppl. 245: 313, 1959.
17. Hulting, B., and Vendsalu, A.: Coarctation of Aorta in Unusual Sites, Acta radiol. 43: 453, 1955.
18. Inmon, T. W., and Pollock, B. E.: Coarctation of the Abdominal Aorta; Review of the Literature, Am. Heart J. 52: 314, 1956.
19. Kondo, B., Winsor, T., Raulston, B. O., and Kuroiwa, D.: Congenital Coarctation of Abdominal Aorta; Theoretically Reversible Type of Cardiac Disease, Am. Heart J. 39: 306, 1950.
20. Martin, J. F., and Yount, E. H.: Coarctation of the Abdominal Aorta. Report of a Case Illustrating the Value of Aortography as a Diagnostic Aid, Am. J. Roentgenol. 76: 782, 1956.
21. Maycock, W. d'A.: Congenital Stenosis of Abdominal Aorta, Am. Heart J. 13: 633, 1937.
22. Power, J. H.: Observations on Disease of Aortic Valves Producing Both Constriction of Aortic Orifice and Regurgitation Through It Into the Left Ventricle Accompanied With Abnormal Enlargement of Two Internal Mammary Arteries and Atrophy of Abdominal Aorta and Its Iliac Branches, Dublin Quart. J. Med. 32: 314, 1861.
23. Quain, R.: Partial Contraction of the Abdominal Aorta, Tr. Path. Soc. London 1: 244, 1846-1848.
24. Reifenstein, G. H., Levin, S. A., and Gross, R. E.: Coarctation of the Aorta. A Review of 104 Autopsied Cases of the "Adult Type," 2 Years of Age or Older, Am. Heart J. 33: 146, 1947.
25. Ritchie, H. D., and Douglas, D. M.: Atresia of the Abdominal Aorta, Brit. M. J. 1: 144, 1956.
26. Rob, C. G., and Vollmar, J. F.: Die Chirurgie der Bauchaorta, Ergebn. chir. Orthop. 42: 1959.
27. Schwartz, M. B., Kniep, C. H., and Schamroth, L.: Congenital Atresia of the Abdominal Aorta, Am. Heart J. 54: 605, 1957.
28. Senning, Å.: Strip-Graft Technique, Acta chir. scandinav. 118: 81, 1959.
29. Sloan, R. D., and Cooley, R. N.: Coarctation of Aorta, Radiology 61: 701, 1953.
30. Steele, J. M.: Evidence for General Distribution of Peripheral Resistance in Coarctation of Aorta; Report of 3 Cases, J. Clin. Invest. 20: 473, 1941.
31. Wang, H. W.: Hypertonie bei circumscripter Stenose der Bauchaorta, Cardiologia 15: 30, 1949.

THE SURGICAL CORRECTION OF SYPHILITIC AORTIC INSUFFICIENCY

Jerome P. Murphy, M.D., Omaha, Nebr.

Despite the numerous operations proposed for the correction of aortic insufficiency, no single procedure has yet evolved which can be effectively and safely applied to the majority of patients in need of assistance. Among the various methods advanced to date, the most widely accepted is the technique of Hufnagel for the placement of a unidirectional flow valve in the descending aorta. When properly done, this operation affords significant palliation and may be a lifesaving measure in selected cases.[1] Unfortunately, this method has serious limitations, exclusive of the operative mortality, as the relief in diastolic reflux is incomplete and at the expense of coronary filling. The indications for this and other operations of a similar nature are not well established and are beyond the scope of this presentation which is a description of a simple and safe means for the correction of aortic insufficiency of syphilitic origin.

The majority of operations for the alleviation of aortic insufficiency are based on the assumption that the aortic valve cusps have been irreparably damaged. This is generally correct with the exception of insufficiency of syphilitic origin.[2] The standard textbooks of pathology describe the events leading to regurgitation as beginning with the spirochetal invasion of the tunica media in the ascending aorta which subsequently undergoes fusiform dilatation.[3] The retrograde extension of this process causes the valve annulus to enlarge symmetrically and functional insufficiency begins with the failure of the valve cusps to coadapt.[2] Progressive regurgitation increases the diastolic capacity of the ventricle with further annular widening, and the fatal cycle is established. The valve cusps undergo fibrotic changes with some nodular thickening and the adjacent aortic wall shows intimal thickening which may cause narrowing of the coronary ostia.[4] This latter change is said to be the cause of the anginal syndrome with eventual myocardial failure. To ascertain the effect of these changes on valve function, a number of syphilitic hearts were studied and it was apparent that the cusps had suffered little loss of motility and the coronary ostia were only slightly narrowed. These observations formed the basis of a new concept for treatment of aortic insufficiency, which consists of plication of the aortic annulus rather than the use of substitute valvular prosthesis. A study of fresh hearts demonstrated the feasibility of this approach

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From the Cardiopulmonary Laboratory and the Department of Surgery, Creighton Memorial, St. Joseph's Hospital, Omaha, Nebr.

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which consists of the circumferential dissection of the root of the aorta and isolation of the coronary vessels allowing for the placement of an external ligature at the level of the annulus, passing below the left and just above the right coronary artery. Controlled plication should diminish or abolish regurgitation without impingement on the coronary vessels or production of outflow obstruction. The degree or amount of narrowing is easily determined by means of continuous pressure recordings from the left ventricle and aorta. After proper placement of the ligature, constriction is carried to that point where the diastolic pressure enters the normal range without production of a systolic gradient across the aortic valve area. The simplicity of this procedure is further enhanced by the ready accessibility of the aortic root through a median sternotomy which avoids the violation of either pleural cavity.

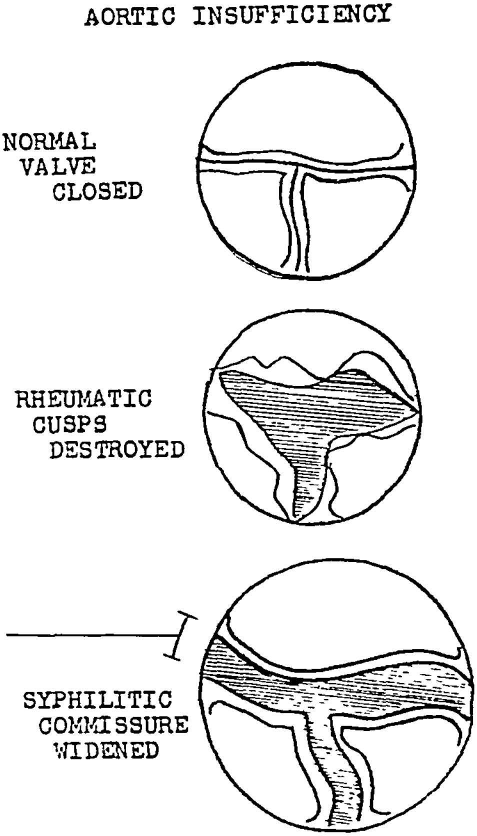

Fig. 1.

The case report which follows is a description of the first clinical application of this technique.

CASE REPORT

On May 1, 1959, a 59-year-old white man was admitted to St. Joseph's Hospital for treatment of intractible heart failure secondary to aortic insufficiency of syphilitic origin.

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Intensive cardiac treatment with digitalis and diuretics failed to alter the downhill course and the patient required continuous oxygen therapy.

Physical evaluation revealed a blood pressure of 220/0 mm. Hg in both arms with all the classical signs of extreme aortic regurgitation manifest in the peripheral pulses. There was a massive precordial heave with extreme cardiomegaly. A Grade 5 aortic diastolic murmur was present with a soft short systolic blow. Cardiac fluoroscopy revealed a linear calcification of the aortic arch with a large heaving left ventricle. The electrocardiogram showed left ventricular hypertrophy and strain.

Despite the extreme dyspnea, the patient's chief complaint was the constant pulsatile body motion which shook the bed with each heartbeat.

On May 25, surgical consultation was secured in order to consider the insertion of a Hufnagel valve. This approach was rejected because of the intractable heart failure. However, as death was imminent it was elected to undertake plication of the aortic annulus.

Surgery, carried out on May 25, consisted of isolation of the aortic root through a median sternotomy. On opening the pericardium, the left ventricle and ascending aorta were found to be massively enlarged. The coronary vessels and the right heart were not abnormal. A direct pressure from the brachial artery was 220/10 mm. Hg. Catheters placed in the aorta gave an identical reading and left ventricular pressure averaged 210-200/15-10 mm. Hg. Pressures taken by cuff over the left brachial artery were identical to the aortic pressure. The base of the annulus was dissected circumferentially and an umbilical tape was passed along this tract coursing below the left or posterior coronary artery and above the right. Progressive narrowing of the tape was caried out until the diastolic pressure reached 40 mm. Hg. The systolic pressure fell simultaneously from 220 to 140 mm. Hg. After securing the knot, a second and a third tape were passed over the same tract and narrowed until the diastolic pressure reached 80-70 mm. Hg. At this point. the systolic reading was 120 mm. Hg in the aorta and left ventricle (Fig. 2). These pressures were considered an endpoint, having restored a normal blood pressure without producing an aortic stenosis. The patient's condition remained good throughout the entire procedure and no arrythmias were noted. The sole alarming feature was the post-plication appearance of the aortic root which was reduced to normal size at the valve but massively dilated above this point. This abrupt transition in caliber was accompanied by a systolic thrill which was not present before surgery and doubtless represented the turbulent change in a post-stenotic dilatation. In this instance the stenosis did not represent physiologic obstruction.

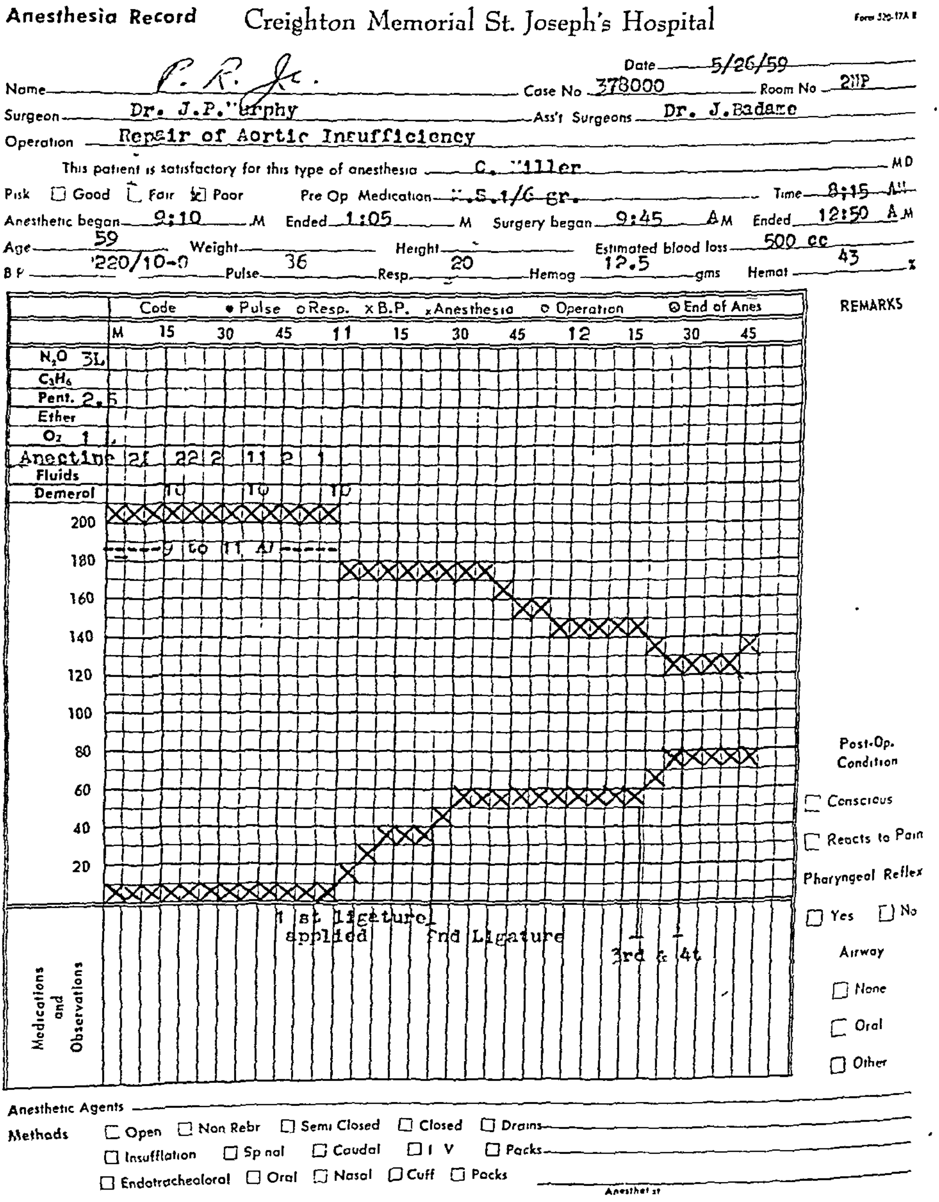
The postoperative course was complicated by a minor wound disruption but otherwise was uneventful. The diastolic murmur was no longer heard but was replaced by a soft systolic component. All signs of heart failure rapidly disappeared as did the pulsatile body motion. For this last relief, the patient was most grateful. On release from the hospital, brachial pressures averaged 140/80-60 mm. Hg. Five months later, pressures averaged 160-140/85-75 mm. Hg. The patient is free of all signs and symptoms of heart failure and has not received any cardiac therapy since leaving the hospital. X-ray studies show a significant diminution in the cardiac silhouette, although some left ventricular hypertrophy remains. The electrocardiogram has undergone a marked change; there is loss of the strain pattern. although some left heart hypertrophy is apparent.

SUMMARY

The pathologic abnormality resulting in aortic regurgitation secondary to syphilitic aortitis does not necessarily involve a loss of valve substance or cusp motility but, rather, consists primarily of a dilatation of the aortic annulus.

Restoration of valvular competence is best accomplished by plication of the annulus rather than the use of valve prothesis.

The initial diagnosis of neurovascular syphilis had been made 10 years previously, at which time active antisyphilitic therapy was carried out. Examination revealed bilateral primary optic atrophy with neurogenic bladder and an aortic insufficiency of moderate degree in a compensated myocardium. The first symptoms of left ventricular failure did not appear until 6 months before hospitalization. At that time, medical therapy was begun with marked symptomatic relief until 1 month before admission when nocturnal dyspnea developed with anasarca and other signs of advanced congestive heart failure.



Anesthesia Record Creighton Memorial St. Joseph's Hospital Form 326-17A E

Date 5/26/59
Name P. R. Jr. Case No 378000 Room No 211P
Surgeon Dr. J.P. "urphy Ass't Surgeons Dr. J.Badame
Operation Repair of Aortic Insufficiency
This patient is satisfactory for this type of anesthesia C. "iller MD
Risk ☐ Good ☐ Fair ☒ Poor Pre Op Medication ".S.1/6 gr. Time 8:15 AM
Anesthetic began 9:10 M Ended 1:05 M Surgery began 9:45 AM Ended 12:50 AM
Age 59 Weight Height Estimated blood loss 500 cc
B P 220/10-0 Pulse 36 Resp. 20 Hemog 12.5 gms Hemat 43 %

Post-Op. Condition
☐ Conscious
☐ Reacts to Pain
Pharyngeal Reflex
☐ Yes ☐ No
Airway
☐ None
☐ Oral
☐ Other

Anesthetic Agents
Methods ☐ Open ☐ Non Rebr ☐ Semi Closed ☐ Closed ☐ Drains
☐ Insufflation ☐ Spinal ☐ Caudal ☐ I V ☐ Packs
☐ Endotracheal oral ☐ Oral ☐ Nasal ☐ Cuff ☐ Packs
Anesthetist

Fig. 2

THE EFFECT OF TOTAL BODY PERFUSION UPON CARDIAC OUTPUT AND VASCULAR RESISTANCE

Howard Rowen, M.D., Peter Viles, M.D.,* and Jay L. Ankeney, M.D.,*
Cleveland, Ohio

INTRODUCTION

Hypotension usually follows extracorporeal perfusion in animals and is also observed in patients. Previous work from this laboratory[1] demonstrated that decreased peripheral flow and vascular resistance play a part in this post-perfusion decrease in systemic pressure. As a continuation of this study, the following experiments were carried out in order to determine the relative roles of cardiac output and total body vascular resistance in hypotension following cardiopulmonary bypass.

METHODS

Healthy mongrel dogs, weighing between 14.0 and 19.5 Kg., were anesthetized with intravenous thiamylal, 12.5 mg. per kilogram. Following intubation, respiration was maintained with an intermittent positive pressure respirator using room air. The left chest was opened through the fifth intercostal space, No. 20 Fr. catheters were inserted into the venae cavae, and the left femoral artery was cannulated. Heparin, 12 mg. per kilogram, was given intravenously. The descending aorta was cross-clamped for less than 2 minutes and a Gregg-type rotameter[7] was inserted just distal to the left subclavian artery. The brachiocephalic and left subclavian arteries were cannulated and connected to the distal limb of the rotameter in such a way that the cerebral blood supply was never completely interrupted. Thus, the entire cardiac output was directed through the flow meter, with the exception of coronary flow. Mean arterial, central venous, and left ventricular pressures were measured with strain gauge transducers and recorded simultaneously with electrocardiogram and cardiac output on a photographically recording oscilloscope. The rotameter was calibrated with blood from the extracorporeal system at the conclusion of each experiment.

Total vascular resistance was calculated by dividing the mean aortic pressure in millimeters of mercury by the cardiac output in cubic centimeters per minute and multiplying the dividend by 100.

From the Department of Surgery, Western Reserve University School of Medicine, and University Hospitals of Cleveland, Cleveland, Ohio

Work supported by a grant from the Cleveland Area Heart Society.

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*Work done in partial fulfillment of the requirements for the M.D. degree, Western Reserve University.

A simple and safe technique for annular plication is described, together with a summary of the first clinical application with this method.

ADDENDUM

The patient was examined 13 months after the operation. His condition remains excellent.

REFERENCES

1. Hufnagel, C. A.: Surgery of Acquired Diseases of the Cardiac Valves, Gen. Pract., East St. Louis 7: 69-81, 1953.
2. Rushmer, R. F.: Cardiac Diagnosis. A Physiologic Approach, Philadelphia, 1956, W. B. Saunders Company.
3. Boyd, W.: Pathology of Internal Diseases, ed. 5, Philadelphia, 1950, Lea & Febiger. pp. 47-48.
4. Gould, S. E., editor: Pathology of the Heart, Springfield, Ill., 1953, Charles C Thomas, Publisher, p. 764.

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*Work done in partial fulfillment of the requirements for the M.D. degree, Western Reserve University.

Table I. Cardiac Output and Aortic Pressure Before and After Control and Perfusion Periods

	EXPT. NO.	PRESSURE (MM. Hg)				CARDIAC OUTPUT (C.C./MIN.)			
		CONTROL		PERFUSION		CONTROL		PERFUSION	
		BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER
High Flow Rate (100 c.c./Kg./min.)	176	75	74	76	72	340	750	420	200
	178	89	88	90	55	850	650	1,400	400
	185	88	88	90	71	925	775	1,000	400
	188	77	90	84	55	1,475	1,500	1,280	780
	189	79	103	100	60	1,320	1,200	1,200	900
Mean ± S.D.*		82 ± 6	89 ± 10	88 ± 9	63 ± 8	980 ± 450	975 ± 400	1,060 ± 385	535 ± 290
Low Flow Rate (50 c.c./Kg./min.)	179	65	70	70	56	400	400	500	475
	180	68	75	69	36	900	700	960	250
	181	74	80	102	35	550	475	850	150
	183	86	91	79	40	890	1,190	1,100	550
	186	88	90	90	65	625	590	700	400
Mean ± S.D.		76 ± 10	82 ± 9	82 ± 14	56 ± 20	675 ± 215	670 ± 310	825 ± 170	365 ± 165
Mean ± S.D. (combined experiments)		79 ± 9	85 ± 10	85 ± 11		830 ± 370	830 ± 355	940 ± 345	

*Standard deviation.

$$\text{Total Vascular Resistance} = \frac{\text{Mean Aortic Pressure}}{\text{Cardiac Output}} \times 100.$$

This abbreviated Poiseuille's equation yields a number which indicates relative degrees of vascular resistance. Since a linear relationship between pressure and resistance does not obtain,[5] resistances were compared at equal pressures for purposes of accuracy.

Cardiac output was recorded and total vascular resistance calculated at various arterial pressures before and after a 30-minute pre-perfusion control period. Similar measurements were made after a 30-minute perfusion period. Arterial pressures were varied during these experimental periods by adding or removing blood from the animal.

Cardiopulmonary bypass was carried out utilizing 100 per cent oxygen in a rotating disk oxygenator, previously primed with 2,500 c.c. of freshly drawn, heparinized blood. Five animals were perfused at rates of 100 c.c. per kilogram per minute (high flow group) and 5 animals at rates of 50 c.c. per kilogram per minute (low flow group). Since blood lost from the operative field was returned to the extracorporeal circuit, by comparing the pre- and post-perfusion circuit volume, the amount of blood lost or pooled by the animal was determined.

Venous and arterial blood samples were drawn at the beginning and end of the perfusion period and analyzed for packed cell volume, pH, oxygen and carbon dioxide content. Oxygen and carbon dioxide content were determined by the method of Van Slyke and Neill,[10] and carbon dioxide tension was calculated using the normogram of Van Slyke and Sendroy.[11]

RESULTS

Detailed data obtained in individual animals during the various experimental periods are reported in Table I (cardiac output and arterial pressure) and in Table II (total vascular resistance). These tables may be referred to for specific data but the results are summarized in Tables III through V and Fig. 1. Since cardiac output, aortic pressure, and total vascular resistance did not change significantly during the pre-perfusion control period in any of the ten experiments, they were combined and listed as a single control group in Fig. 1 and the tables summarizing the results.

In all 10 animals, hypotension followed extracorporeal perfusion (Table III). In the high flow group, the average pressure fall was from 85 mm. Hg before perfusion to 63 mm. Hg following perfusion. In the low flow group, the average pre-perfusion pressure was 85 mm. Hg, falling to 56 mm. Hg immediately after perfusion.

Cardiac output (Table IV) in the high flow group fell from a pre-perfusion level of 940 to 535 and in the low flow group from 940 to 365 c.c. per minute in the immediate post-perfusion period. The decreases in pressure and output as a result of bypass are statistically significant as indicated in Tables III and IV.

Table V shows the effect of perfusion upon total body vascular resistance. Resistance did not change significantly in the high flow group as compared to control values. But on the other hand, resistance was significantly reduced below control levels following low flow perfusion.

TABLE II. PER CENT CHANGE IN RESISTANCE FOLLOWING CONTROL AND PERFUSION PERIODS

	EXPT. NO.	% CHANGE IN RESISTANCE	
		CONTROL PERIOD	POST-PERFUSION
High Flow Group (100 c.c./Kg./min.)	176	− 1	+82
	178	+23	+33
	185	+42	+24
	188	− 9	+25
	189	+26	−36
Mean ± S.D.*		+16 ± 20	+26 ± 45
Low Flow Group (50 c.c./Kg./min.)	179	− 7	−30
	180	+ 3	−36
	181	+ 9	−48
	183	—	—
	186	+12	−30
Mean ± S.D.		+4 ± 8	−32 ± 3
Mean ± S.D. (combined experiments)		+11 ± 17	

*Standard deviation.

TABLE III. EFFECT OF PERFUSION ON ARTERIAL PRESSURE

	PRESSURE (MM. Hg)			
	COMBINED CONTROL		PERFUSION	
	BEFORE	AFTER	BEFORE	AFTER
High Flow	79 ± 9	85 ± 10	85 ± 11	63 ± 8 $p < 0.001$
Low Flow			85 ± 11	56 ± 20 $p < 0.002$

TABLE IV. EFFECT OF PERFUSION ON CARDIAC OUTPUT

	CARDIAC OUTPUT (C.C./MIN.)			
	COMBINED CONTROL		PERFUSION	
	BEFORE	AFTER	BEFORE	AFTER
High Flow	830 ± 370	830 ± 355	940 ± 345	535 ± 290 $p < 0.02$
Low Flow			940 ± 345	365 ± 165 $p < 0.001$

TABLE V. EFFECT OF PERFUSION ON TOTAL VASCULAR RESISTANCE

	% CHANGE IN TOTAL VASCULAR RESISTANCE	
	CONTROL PERIOD	POST-PERFUSION
High Flow	+11 ± 17	+26 ± 45
		$p < 0.003$
Low Flow		−32 ± 3 $p < 0.001$

A graphic presentation of the effect of perfusion upon cardiac output, aortic pressure, and total vascular resistance is shown in Fig. 1. This graph clearly shows, as indicated above, that there is a significant fall in aortic pressure and cardiac output following either high or low flow cardiopulmonary bypass. Total vascular resistance on the other hand, rises somewhat (not significantly) following high flow perfusion, but falls following one-half hour of perfusion at 50 c.c. per kilogram. This graph also demonstrates that during the 30-minute period of observation before perfusion, the animals were all quite stable.

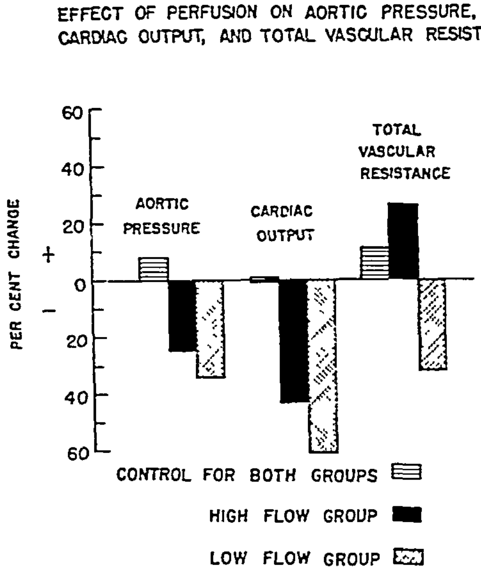

Fig 1

Both groups of animals were comparable as regards pH, arterial and venous oxygen saturation, arterial carbon dioxide tension, and hematocrit at the end of perfusion. Eight of 10 dogs pooled blood during perfusion, the high flow group tending to pool more blood than the animals in the low flow group. In no experiment was there a significant elevation of central venous pressure or left ventricular end diastolic pressure.

DISCUSSION

Previous measurements of resting cardiac output in closed chest dogs have been in the range of 100 c.c. per kilogram per minute.[4, 9] In our experiments, cardiac output was measured in anesthetized animals prepared for cardiopulmonary bypass and was found to be in the range of 50 c.c. per kilogram per minute. This latter figure is comparable to cardiac output in open heart preparations reported elsewhere,[2, 4, 6, 8] and can probably be explained by loss of negative intrathoracic pressure[3] and the trauma of surgery, including blood loss, catheters in the venae cavae, and vascular reflex changes.

Hypotension followed perfusion in all 10 animals and was primarily due to a decrease in cardiac output. This decreased cardiac output could be the result of (1) myocardial failure or (2) a decreased effective circulating blood volume. Cardiac failure did not appear to be a factor, since at no time was there any elevation of left ventricular end diastolic or central venous pressure.

Therefore, a decreased effective circulating blood volume was probably responsible for this diminished cardiac output. Consistent with this conclusion is the fact that all animals responded to transfusion of small amounts of whole blood by increasing cardiac output and aortic pressure toward control levels. This diminished blood volume is not the result of external blood loss but is probably due to the fact that the animals pooled sizeable quantities of blood during perfusion. This blood absorbed by a perfused animal must be sequestrated in inaccessible vascular pools. Work in progress in our laboratory indicates that the liver is one of the sites for this blood sequestration.*

Decreased post-perfusion total body vascular resistance also contributed to hypotension in the low flow group whereas the animals perfused at their estimated resting cardiac output (100 c.c./Kg./min., high flow group) were able to maintain their vascular resistance. There were no differences in body temperature, pH, arterial or venous oxygen saturation or arterial carbon dioxide tension between the high and low flow groups to account for this fall in resistance.

The results of these experiments have definite clinical application. First, the fact that low perfusion flow rates result in a loss of vascular tonus emphasizes the importance of maintaining as high a perfusion rate as possible during cardiopulmonary bypass. Furthermore, these experiments show that hypotension following cardiopulmonary bypass is a result of decreased cardiac output due to a diminished effective circulating blood volume. With this experimental evidence in mind, we have found that, following total cardiopulmonary bypass, it is often necessary to discontinue perfusion with a positive blood balance in order to maintain an adequate systemic pressure. In fact, if hypotension is present, blood is given to the patient until the right atrium appears to be slightly distended. In almost every instance, the infusion of additional blood results in maintenance of a normal systemic pressure and adequate cardiac output. If the pressure does not respond to this additional volume of blood before the atrium becomes too distended, vasopressors are then indicated. We have not found it necessary to use vasopressors to maintain systemic pressure in the last 100 clinical cases.

SUMMARY

1. Cardiac output, aortic, left ventricular and venous pressures were measured during 30 minutes of control and after a half-hour period of extracorporeal bypass in animals.

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*To be published

2. In 5 animals (high flow group), arterial perfusion rate was 100 c.c. per kilogram per minute and, in 5 animals (low flow group), the rate was 50 c.c. per kilogram per minute.

3. Hypotension and decreased cardiac output followed perfusion in all animals.

4. This hypotension and decreased cardiac output are probably due to a decreased effective circulating blood volume as a result of blood pooling.

5. Perfusion rate of 50 c.c. per kilogram per minute resulted in a decrease in total body vascular resistance, but resistance remained unchanged following high flow perfusion rate.

6. The results of these experiments emphasize the importance of maintaining high flow rates and explain the rationale for maintaining a positive blood balance following extracorporeal bypass.

REFERENCES

1. Ankeney, J. L., Viles, P. H., and Leonards, J. R.: A Study of Changes in Peripheral Flow and Resistance as Associated With Total Body Perfusion, S. Forum 9: 157, 1958.
2. Berglund, E.: Balance of Left and Right Ventricular Output: Relation Between Left and Right Atrial Pressures, Am. J. Physiol. 178: 381, 1954.
3. Brecher, G. A., and Mixter, G.: Effect of Respiratory Movements on Superior Cava Flow Under Normal and Abnormal Conditions, Am. J. Physiol. 172: 457, 1953.
4. Ferguson, T. B., Shadle, W., and Gregg, D. E.: Effect of Blood and Saline Infusion on Ventricular End Diastolic Pressure, Stroke Work, Stroke Volume and Cardiac Output in the Open and Closed Chest Dog, Circulation Res. 1: 62, 1953.
5. Green, H. D., Lewis, R. N., Nickerson, N. D., and Heller, A. L.: Blood Flow, Peripheral Resistance and Vascular Tonus, With Observations on the Relationship Between Blood Flow and Cutaneous Temperature, Am. J. Physiol. 141: 518, 1944.
6. Schwartz, S. I., DeWeese, J. A., Niguadula, F. N., Gabel, P. V., and Mahoney, E. B.: Tissue Oxygen "Tension" at Various Flow Rates of Extracorporeal Circulation, S. Forum 9: 151, 1958.
7. Shipley, R. E., and Wilson, C.: An Improved Recording Rotameter, Proc. Soc. Exper. Biol. & Med. 78: 724, 1951.
8. Wegria, R., Rojos, A. G., and Wiggers, C. J.: A Study of Spontaneous Fulminant Shock in the Heart-Lung-Dog Preparation, Am. J. Physiol. 138: 212, 1942.
9. Wiggers, C. J.: Cardiac Output and Total Peripheral Resistance Measurements in Experimental Dogs, Am. J. Physiol. 140: 519, 1943.
10. Van Slyke, D. D., and Neill, J. M.: The Determination of Gases in Blood and Other Solutions by Vacum Extraction and Manometric Measurement, J. Biol. Chem. 61: 523, 1924.
11. Van Slyke, D. D., and Sendroy, J. J.: Studies of Gas and Electrolyte Equilibria in Blood, J. Biol. Chem. 79: 781, 1928.

AUTOGENOUS OXYGENATION WITH CARDIAC BYPASS, HYPOTHERMIA, AND AN ATRIOVENTRICULAR CLAMP

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THE RECENT REBIRTH of interest in autogenous oxygenation with bypass during cardiac surgery is the natural product of a desire to achieve the ideal method of cardiac isolation.

We have used autogenous oxygenation with rapid cooling to allow cardiotomy at low temperatures while perfusion is stopped[12] and now present a method that permits cardiotomy during autogenous oxygenation without interruption of perfusion. This system depends upon the use of a clamp which interrupts blood flow at the atrioventricular level.

There have been a number of other attempts in the past to use autogenous oxygenation for intracardiac surgery. In 1950, Sirak[13] employed experimental left atrial cannulation with a diaphragm occlusion of the mitral valve to provide a bloodless left ventricle. Since then numerous investigators, notably Potts,[10] Wesolowski,[14] Cohen,[4] Campbell,[3] Read,[11] and more recently Blanco,[1] Mustard,[9] Helmsworth,[7] Shields and Lewis,[12] and Drew[5, 6] and their associates have attempted to utilize the natural medium of oxygenation for open-heart surgery. Their results have varied considerably, with the most consistent problems involving left atrial drainage, pulmonary edema, the need for intracardiac catheters, and difficulties in producing dry intraventricular fields.

Our present study on this subject was directed toward further perfection of the technique of bilateral cardiac bypass and determination of the maximum safe period of ventricular ischemia with the use of a special atrioventricular clamp, profound hypothermia, and autogenous oxygenation.

MATERIALS AND METHODS

A total of 50 adult mongrel dogs, whose average weight was 30 pounds (13.6 Kg.), were subjected to cardiac bypass under Sodium Pentothal (27.5 mg./Kg.) anesthesia and artificial ventilation with 100 per cent oxygen.

Thoracotomy was performed through the fourth left intercostal space and after heparinization (2 mg./Kg.), cannulations shown in Fig. 1 were carried

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out. The pulmonary artery was cannulated approximately 1.5 cm. distal to the pulmonary valve using a double purse-string suture and a 16 Fr. catheter (Fig. 2). The right and left atria were cannulated via the auricular appendages using 24 Fr. Bardic catheters with multiperforated steel inserts (Fig. 4, *d*). A 14 to 16 Fr. catheter was inserted in the femoral artery.

On completion of the bypass, 100,000 units of penicillin was injected into the free pleural cavity. A chest tube drainage was used for 2 to 3 hours. Postoperatively, intramuscular injections of 100,000 units of penicillin were given daily for 3 to 4 days.

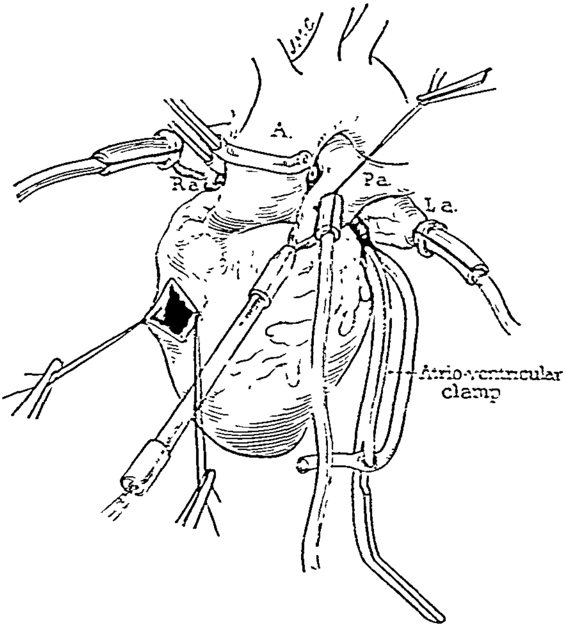

Fig. 1.—Drawing which shows cannulated heart during total bypass and ventricular isolation. Atrioventricular clamp is seen compressing both inflow tracts on atrial side of A-V groove. Femoral artery cannula is not pictured.

Two identical pump bypass units,[8] similar to those described previously,[12] were used (Fig. 3). Sealed plastic bag reservoirs were used instead of open Lucite cylinders. The distensibility of the plastic bags allowed the use of a simple volume detector which activated a relay system to operate the blood pumps, thus providing semi-automatic control which permitted the use of a small extracorporeal blood volume (600 c.c.). De Bakey or Sigmamotor pumps were used. Each pump unit was primed with 300 c.c. of fresh heparinized whole blood (30 mg. per liter). Following the bypass, the heparin was neutralized by intravenous injection of Polybrene (1 mg. for each milligram of heparin given prior to bypass).

In the first 15 experiments, cooling and rewarming was accomplished by the immersion of two 15 feet coils of stainless steel tubing interposed, one in each pump circuit, in pails of salt-ice-water solution (0° C.) followed by warm water (45° C.).

The 35 remaining experiments were conducted using a Brown-Sealy blood heat exchanger[2] which cooled either the systemic or pulmonic circuits. The temperature of this device was regulated by the circulating fluid of an Autotherm* machine. This device integrates electronically the subject's temperature with a variable desired temperature to cause the circulating fluid to cool or warm the subject to the desired temperature. The minimum cooling fluid temperature was 6° C., while the maximum warming temperature was 44° C. Rewarming was aided by use of a Therm-O-Rite blanket at 46° C.

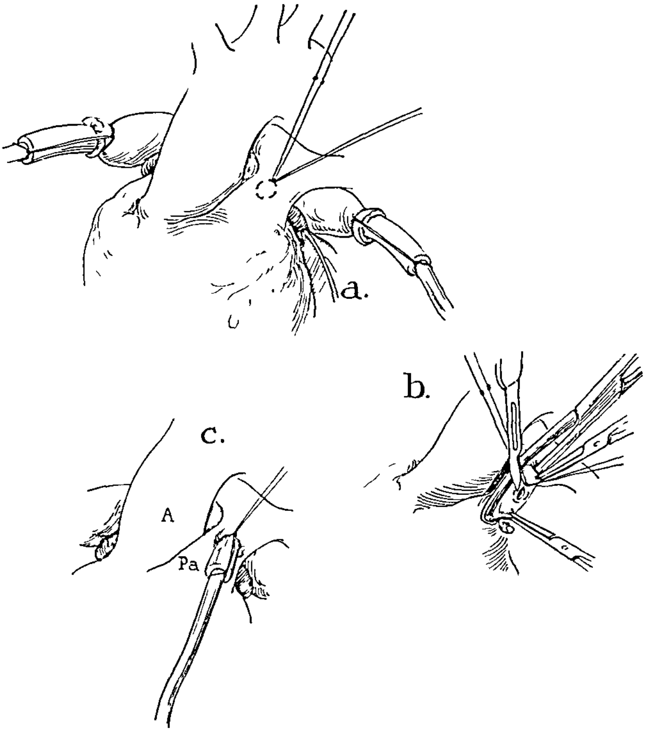

Fig. 2.—Drawing which shows steps in cannulation of pulmonary artery.

a, Double-stranded purse-string suture in pulmonary artery.

b, After hemostat traction on pulmonary artery adventitia, a Beck aorta-type clamp is applied to isolate purse string in pulmonary artery. An arteriotomy is then made as shown and the cannula is inserted.

c, One strand of purse string is tied to anchor cannula. Remaining purse string is tied following removal of cannula to close arteriotomy with negligible stenosing.

In several experiments the pleural cavity was irrigated with cold (6 to 10° C.) saline to accelerate the cooling rate and to provide local heart cooling.

Isolation of both ventricles was achieved by occlusion of inflow and outflow tracts. The inflow occlusion was simple and by allowing uninterrupted filling of the atria could be continued during ventriculotomy or aortotomy. This inflow occlusion was accomplished by applying tension to a rubber tube lying within the transverse cardiac sinus and attached at one end to a metal bar which was in contact with the atria posteriorly in the oblique sinus. The free end

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*Autotherm Corp., West Los Angeles, Calif.

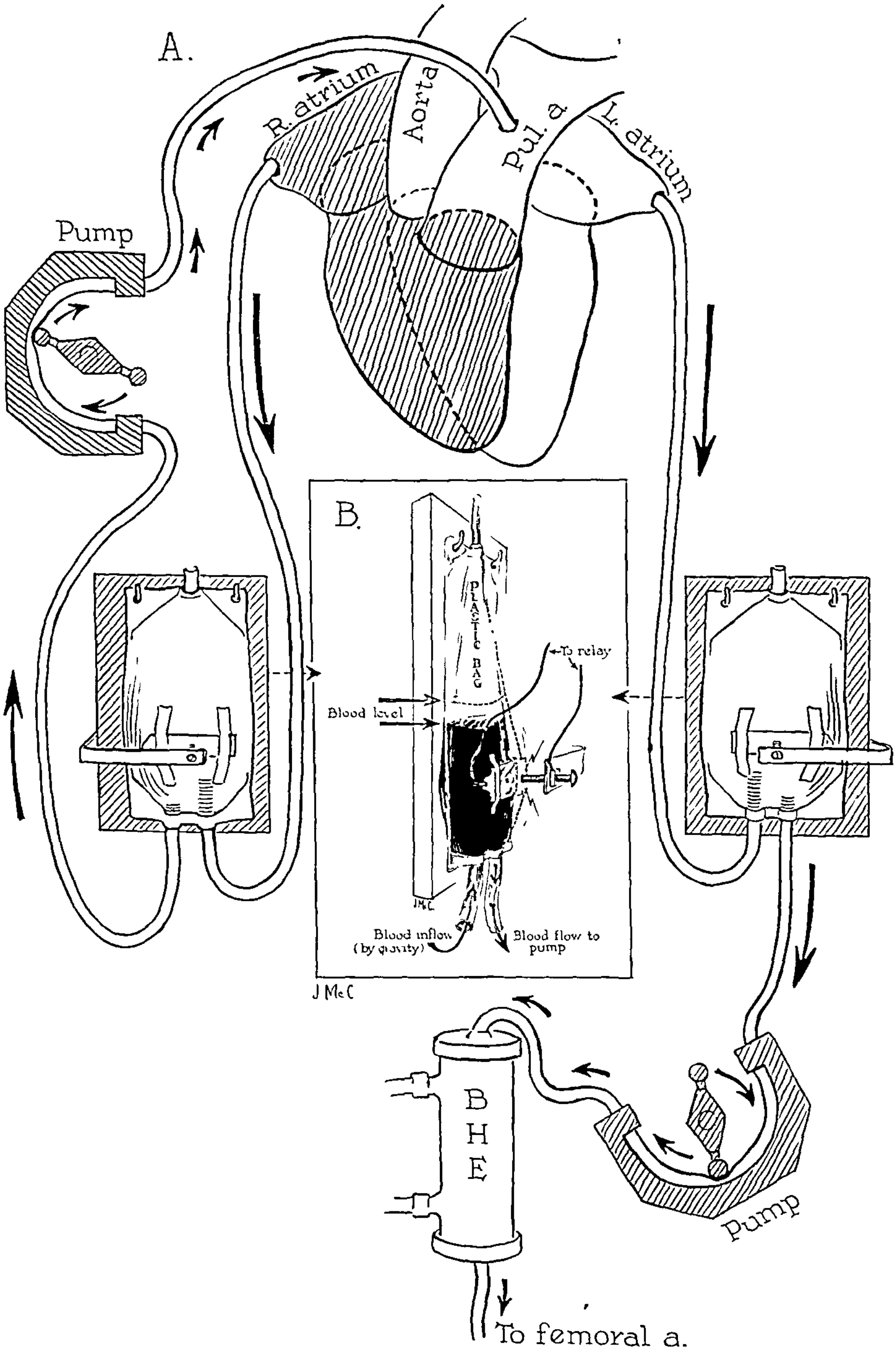

Fig. 3.—*A*, Schematic drawing of bypass system with two pump units showing plastic bag reservoirs with attached volume detector, automatically controlled pumps, and blood heat exchanger.

B, Detailed drawing of reservoir and volume detector.

of the rubber tube was then anchored in a notch in the metal bar, resulting in complete occlusion of the atria on the atrial side of the coronary sulcus without serious limitation of the atrial capacities (*Fig.* 4, *b* and *c*).

Following inflow occlusion, the ascending aorta was cross-clamped with a clamp of the Blalock type. The pulmonary artery was occluded proximal to the catheter with a rubber-tipped glass tube umbilical tape tourniquet. A right ventriculotomy was performed in all cases to ascertain the effectiveness of the inflow clamp.

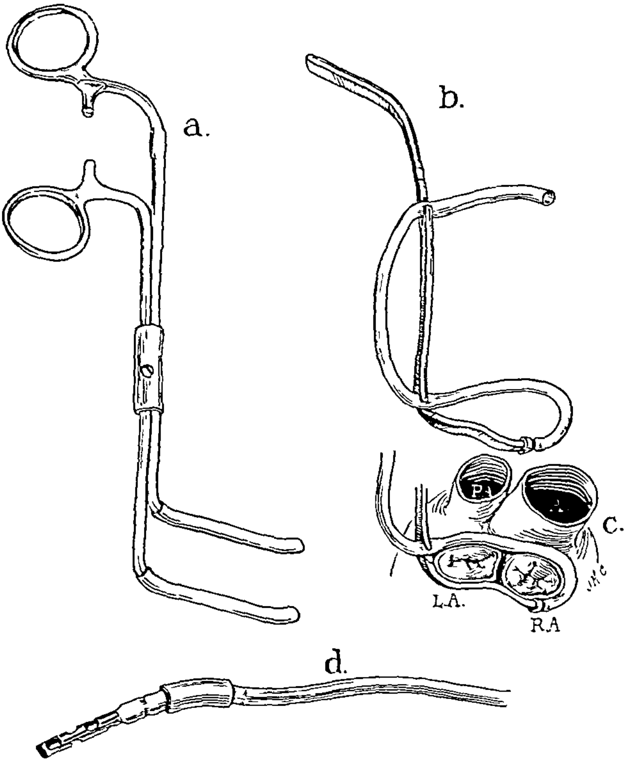

Fig. 4.—*a*, Rubbed-sleeved compression atrioventricular clamp.
b, Rubber tube traction atrioventricular clamp.
c, Clamp *b* applied around atria.
d, Atrial cannula with multiperforated metal insert.

Atrial occlusion was accomplished when the heart temperature was below 25° C. in the hypothermia experiments. Rewarming was started 10 to 15 minutes before occlusion was released.

In the group of 6 normothermic dogs, cardiac arrest was obtained by injecting potassium citrate solution (4 dogs) or acetylcholine (2 dogs) proximal to the aortic clamp.

Monitoring catheters were routinely inserted into the femoral artery and vein and left atrium for direct pressure readings. Temperatures of the rectum, heart, esophagus, circulating blood in the bypass and Autotherm fluid were recorded. Flow rates of bypass pumps and amounts of blood and saline given during the procedure were also recorded.

Blood samples were drawn for control studies, following the cooling stage, before discontinuing the bypass, and 2 to 3 hours postoperatively. Plasma hemoglobin and pH studies were performed on each sample. In 40 per cent of the experiments, hematocrit, CO_2, pCO_2, O_2 content and per cent of O_2 saturation determinations were taken.

Dogs surviving over 1 week were considered long-term survivors. All dogs were autopsied and specimens were taken for histologic studies.

RESULTS

The 50 experiments were divided into five groups according to the length of ventricular isolation and the blood circuit used for temperature control. The groups of experiments were done in sequence, A through E. The results are summarized in Table I.

TABLE I

	GROUP					
	A	B	C	D	E	TOTAL
Time isolation (min.)	30	30	45	45	60	
Total length of bypass	56 min. 43-62	42 min. 39-48	75 min. 64-85	64 min. 56-72	76 min. 67-85	
Circuit cooled	Both	Normothermic	Systemic	Pulmonic	Systemic	
Number of dogs	15	6	11	7	11	50
Technical deaths	0	1	0	2	2	5
24-hour survivors	11 (74%)	5 (100%)	8 (73%)	4 (80%)	3 (33%)	31 (70%)
7-day survivors	10 (67%)	3 (60%)	8 (73%)	2 (40%)	1 (11%)	24 (53%)
Average heart temp. during cooling	16° C.	32° C.	19° C.	20° C.	20° C.	
Average arterial pressure during bypass (mm./Hg)	82	100	79	80	73	
Average perfusion rate (c.c./min./Kg.)		90	60	70	50	

It will be seen that the mortality was similar at 30 and 45 minutes of ventricular isolation, with an increase in mortality as 60 minutes of isolation was reached. Thirty minutes of cardiac isolation with this system was tolerated quite well even at normal temperature, but 60 minutes resulted in a high mortality rate even with hypothermia added. This may simply indicate that we had reached the limit at which cardiac recovery from ischemia was impossible. In most cases, perfusion of the rest of the animal seemed adequate.

Results of the 50 experiments will be described in the following five categories:

1. *Deaths.*—The five technical deaths in this study resulted from pump or respirator failure. Primary findings in nontechnical deaths were 6 hemothorax, 5 shock, 5 pulmonary complications, 2 neurologic complications, and 3 undetermined. Over half of the deaths from hemorrhage and shock were in the first group during procedure development and in the 60-minute occlusion group. Those succumbing to pulmonary complications were in the normothermic and pulmonary cooling groups.

2. *Pathology.*—The most consistent gross pathologic features seen in the autopsied hearts were organized atrial thrombi along the line of clamp compression in 8 of the 24 long-term survivors and myocardial ecchymosis along the same line in most short-term survivors. These findings were especially marked in the atria clamped with parallel rubber-sleeved metal bars (Fig. 4, *a*) which were used in the early experiments.

Other findings among long-term survivors included myocardial abscesses in 4 dogs, four empyemata, and three single lobe atelectases. Death apparently due to pneumonia in 1 dog was the only known instance of fatality from infection. All 5 dogs in Group B (normothermic occlusion), showed a transition of diffuse red hemorrhagic to brownish discoloration of the ventricular myocardium, depending upon the length of survival.

Hind limb paralysis was noted in 2 short-term survivors. The primary cause of death was not determined.

Histologic study of sections taken through the area of atrial compression revealed fibrous organization in the regions of subendocardial ecchymosis. Liver, lung, and kidney sections showed no consistent pathology and did not help in determining the cause of unexplained deaths.

3. *Blood Pressure.*—Venous and atrial pressure recordings indicated that adequate drainage of both atria can be accomplished with a resultant arterial pressure compatible with life.

Venous (inferior vena cava) pressures showed a consistent pattern. Following occlusion, the pressure would rise approximately 4 cm. of saline and then slowly return to normal or often 3 to 4 cm. below on termination of the bypass.

Pulmonary artery pressures were taken in several instances in Group A and did not exceed 25 mm. Hg during occlusion.

Results of left atrial pressure monitoring indicated that the gravity drainage was adequate, since there was seldom more than a 5 cm. saline pressure increase during occlusion period. On numerous occasions the pressure fell below normal, especially during the last 15 minutes of occlusion in the 45- and 60-minute groups. A potential hazard was seen in the occasional occurrence of a negative left atrial pressure following release of occlusion. In such situations we felt the avoidance of air embolism from a loosely fitting catheter was accomplished by using a double looped 1-0 silk suture tied around the atrial appendage and its contained catheter with an internal supporting metal insert (Figs. 1 and 4, *d*).

The arterial pressure pattern was quite similar in all experiments except the normothermic group. There was a 20 to 30 mm. Hg pressure drop during the cannulation period. A further 30 to 40 mm. Hg drop was seen during the first 5 minutes of the bypass with cooling. The pressure would then rise in response to fluid administration and would remain reasonably constant for 15 to 25 minutes, depending upon whether saline or blood was given. Thereafter, there would be a gradual downward progression only momentarily reversed by fluid administration. This pattern would continue until the warming phase was begun, after which the pressure would rapidly return to the early bypass level. Following release of the occlusion clamps the pressure would again fall precipitously until a partial bypass was established after a regular heartbeat was reinstated by electroshock. In all experiments, the need for fluid was determined by depression of blood pressure below 60 mm. Hg. On discontinuing the bypass, the pressure was usually 40 to 50 mm. Hg below the normal preoperative level. The 6 normothermic dogs maintained a near postcannulation pressure during the entire bypass with a momentary depression following occlusion.

4. *Blood Studies.*—The results of blood studies are seen in Fig. 5. Gas studies were performed with a Van Slyke apparatus. Gas exchange and pH maintenance were satisfactory in all groups with the few exceptions mentioned below. Plasma hemoglobin levels did not reach excessive levels.

The widest fluctuation of pH was in Group C (45-minute occlusion) which was also the group with the highest survival rate. In this group, an average pH value of 7.64 was found following the 30-minute cooling period and 7.24 2 to 3 hours postoperatively. Postoperative acidosis was also evident in Group D and was severe (7.13) in the lowest survival group (E). No attempt was made to correct the pH other than by anticipatory variation of the respiratory rate.

Plasma hemoglobin values followed the expected linear relation to the length of the bypass. In only one group (E), with an average bypass length of 76 minutes, did the mean value exceed 100 mg. per cent. In contrast, Group C, in which bypass averaged 75 minutes, showed less than 100 mg. per cent. The variable in these two groups was an additional 15 minutes of cooling with myocardial ischemia in Group E.

Blood gas studies were unfortunately performed only in Groups A, C, and D. A diminution of both venous and arterial volume per cent CO_2 was seen in all groups except the postoperative samples in Group C, which showed marked elevations.

Satisfactory O_2 saturation was obtained in all cases except in the postoperative samples from Groups C and D. Group C showed a marked venous anoxia of 42 per cent O_2 saturation with an acceptable arterial saturation of 88 per cent. Group D had a similar venous value with a markedly reduced arterial value of 66 per cent, indicating a danger in pulmonary cooling.

5. *General Observations.*—A dry ventricular field was obtained in all instances as shown by a bloodless right ventricle following cardiotomy. An aortotomy was performed in several early experiments which showed, after initial evacuation, a dry aortic valve and left ventricle.

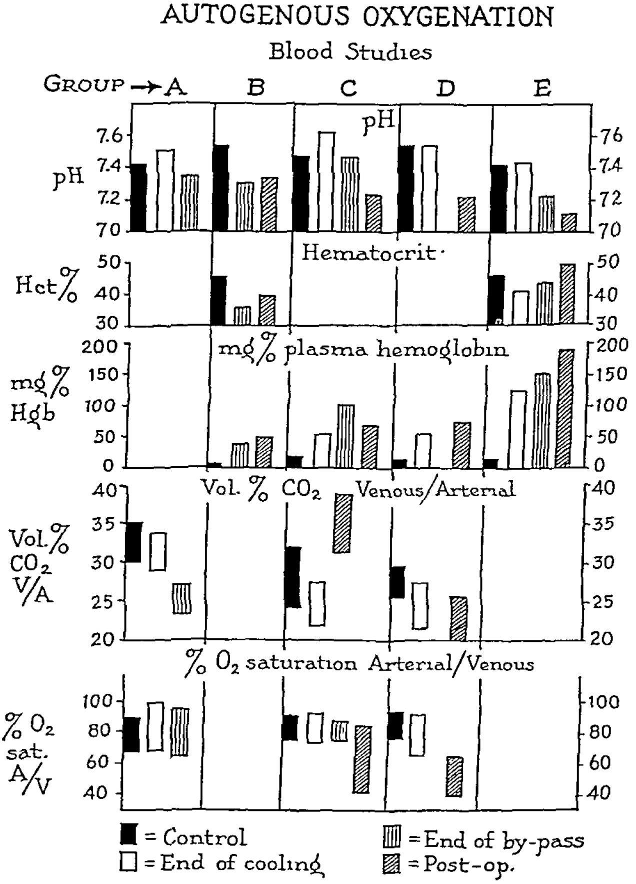

Fig. 5.

Pulmonary edema, as determined by endotracheal aspiration was seen in only 2 experiments; once following acute hemorrhage during cannula removal and once after a 3-minute period of severe shock due to pump failure before hypothermic induction. Both cases were in the pulmonary cooling group and the animals received large amounts of blood (500 c.c.) and saline (1,000 c.c.) to combat their shock.

The heart was seen to fibrillate and pass rapidly into hypothermic arrest at 22 to 25° C. during cooling. On rewarming, fibrillation occurred at 26 to 30° C. and would become quite strong above 30° C. following release of the occlusion clamps. Defibrillation was accomplished with a 0.2 second 115 volt intermittent shock. The period of time required for defibrillation generally varied directly with the length of the occlusion period and seldom exceeded 2 minutes.

Three of the 4 dogs in Group B (normothermic), receiving potassium citrate for cardiac arrest, reverted to normal sinus rhythm following release of occluding clamps without requiring defibrillation. The 2 remaining dogs in this group, having received 200 mg. of acetylcholine, fibrillated during the first 10 minutes of the ventricular isolation period before arrest intervened. Defibrillating shocks were necessary to restore normal sinus rhythm after occlusion release. Electrocardiograms were taken postoperatively in several early experiments and revealed no alteration of the atrial conduction system.

DISCUSSION

The described bypass technique could be used for surgery of the ventricles, including outlet valves, coronary arteries, and ventricular septum below the endocardial cushion. Surgery of the remaining portions of the heart can be performed using a somewhat similar procedure developed in the same laboratory by Shields and Lewis[12] which involves profound hypothermia and circulatory arrest. Drew[6] has successfully applied this procedure clinically.

One of the outstanding features of this bypass technique is the small (600 c.c.) extracorporeal blood volume required. This minimizes the need for special blood preparations and, in some instances, the bypass priming blood could be drawn from the patient immediately before surgery.

Our closed system of bypass circuit eliminated much of the air embolism hazard ever present with heart-lung units and open circulation systems. Blood gas exchange was obviously not a problem.

The use of hypothermia avoided the dangers and difficulties incident to chemical cardiac arrest. The hazards of cardiac malfunction during hypothermia were avoided by partial bypass support during the cooling and rewarming stages.

Table II compares several of the more recent experimental studies on autogenous oxygenation.

TABLE II. EXPERIMENTAL AUTOGENOUS OXYGENATION STUDIES

AUTHOR	NUMBER OF DOGS	LENGTH BYPASS (MIN.)	LENGTH CARDIAC ISOLATION (MIN.)	TEMPERATURE	CARDIOTOMY	24-HOUR SURVIVAL
Cohen & Lillehei[4]	55	10-30	<30	normothermia	5 atria	50 (90%)
Blanco et al.[1]	13	30	none	normothermia	rt. ventricle	10 (77%)
Mustard et al.[9]	15	30-40	<30	normothermia	rt. ventricle	11 (73%)
Helmsworth et al.[7]	52	30	<30	normothermia	rt. ventricle	31 (59%)
Drew et al.[5, 6]	17	?	20-45* (6 dogs)	8-15° C.	?	4 (24%)
Shields & Lewis[12]	55	30-35	10-50*	$<20°$ C.	11 ventricles	26 (47%)
Holt and Lewis	45	40-85	30-60	15° C.	rt. ventricle	31 (70%)

*Total circulatory arrest.

The four most troublesome technical aspects of this study follow:

1. *Arterial Occlusion Clamp.*—A clamp was sought which would totally occlude the ventricular inflow track without traumatizing the atria or seriously compromising their capacity, and which could be readily applied and removed without obstructing the surgical field. Numerous prototypes were tried, two of which are pictured in Fig. 4. Clamps similar to type *a* were applied with the least manipulation of the heart but caused more intra-atrial thrombosis, especially at the two points of compression reflection. Type *b* proved the least traumatic and effectively prevented blood flow to the ventricles. When tension was applied to the rubber tubing in this clamp, the atria were collapsed to some extent in a transverse as well as a longitudinal plane as seen in Fig. 4, *c*. A narrow rubber tube (1/8 in., outer diameter) was found necessary to prevent trauma to the vessels lying within the coronary sulcus and to minimize tension at the ventricular aspect of the auricular-atrial junction. Evidence of atrial trauma resulting from this clamp was a circumatrial ecchymosis and several instances of small (5 mm. diam.) organized intra-atrial thrombi. Although some atrial volume limitation was evident with both clamps, it was not considered serious. Neither clamp imposed restrictions on the immediate surgical field.

2. *Pulmonary Artery Cannulations.*—After trial with transventricular and direct arterial approaches, we found the direct arterial method more satisfactory. The technique which we employed is illustrated and described in Fig. 2.

3. *Arterial Cannulations.*—In the early experiments, considerable difficulty was encountered in preventing the atrial catheters from passing into the ventricles before applying the atrioventricular inflow clamp or preventing kinking of the catheters, especially in the left atrium, after clamping the atria. A solution to this problem and that of potential air embolism or blood loss around the catheters was found in the use of a multiperforated stainless steel tube, 5 cm. in length, inserted in the end of the catheter (Fig. 4, *d*). This rigid tip allowed manipulation of the catheter to provide a patent passage for drainage. The only indication of intra-atrial trauma from the metal insert tip was a localized ecchymosis at the site of prolonged contact in most short-term and several long-term survivors.

4. *Variation in Cardiac Cannulations.*—A partial solution to the problem of cardiac cannulation was found which has limited experimental application but significant clinical appeal. By utilizing a bilateral thoracotomy or median sternotomy approach, the right atrium is cannulated through the right external jugular vein, the left atrium from the right and anterior to the entrance of the right pulmonary veins, and the pulmonary and femoral arteries in the manner previously described. The higher mortality incident to bilateral thoracotomy which we have experienced in dogs precluded the use of this as a routine technique in our laboratory. With this cannulation approach, the pulmonary artery catheter is the only one in the field which can become an obstacle in ventricular surgery and the left atrial catheter is the only one requiring a cardiotomy for insertion. There is, however, an added danger of left atrial air

embolism due to leakage via the purse-string tie of the left atrial catheter. Mention might be made here that generally four catheters are used for pump-oxygenator bypass also.

CONCLUSION

We believe that our system satisfies the criteria for a successful autogenous oxygenation bypass as listed by Mustard,[9] such as (1) adequate oxygenation and exchange with total perfusion, (2) elimination of pulmonary venous obstruction, and (3) dry cardiotomy exposure.

Utilizing the described isolation and bypass system, all portions of the heart are rendered bloodless for surgery with the exception of the atria and the atrioventricular valves. This procedure can be readily modified to permit intra-atrial and atrioventricular valve surgery using the method described by Shields and Lewis[12] and Drew.[5, 6]

SUMMARY

1. Fifty dogs were subjected to bilateral total bypass with autogenous oxygenation and periods of ventricular isolation varying from 30 to 60 minutes while under profound hypothermia (44 dogs) or normothermia (6 dogs).

2. Variations in blood study values associated with a high mortality rate were found only in the group of dogs subjected to 60-minute ventricular ischemia.

3. The 24-hour survival rate in all experiments was 70 per cent and for over 1 week, 53 per cent. A 73 per cent long-term survival rate was obtained in the group with a 45-minute period of ventricular isolation (Group C).

4. Both ventricles, their outlet valves, and coronary arteries were rendered dry for open surgical repair.

REFERENCES

1. Blanco, G., Oca, C., Laguna, S., Nunez, L. E., Schaefer, J., and Bailey, C. P.: Autogenous Lung Oxygenation During Cardiac By-Pass, Am. J. Cardiol. 2: 302, 1958.
2. Brown, I. W., Jr., Smith, W. W., Young, W. G., Jr., and Sealy, W. C.: Experimental and Clinical Studies of Controlled Hypothermia Rapidly Produced and Corrected by a Blood Heat Exchanger During Extracorporeal Circulation, J. THORACIC SURG. 36: 497, 1958.
3. Campbell, G. S., Crisp, N. W., and Brown, E. B., Jr.: Total Cardiac By-Pass in Humans Utilizing a Pump and Heterologous Lung Oxygenation (Dog Lungs), Surgery 40: 364, 1956.
4. Cohen, M., and Lillehei, C. W.: Autogenous Lung Oxygenator With Total Cardiac By-Pass for Intracardiac Surgery, S. Forum 4: 34, 1953.
5. Drew, C. E., Keen, G., and Benozon, D. B.: Profound Hypothermia, Lancet 1: 745, 1959.
6. Drew, C. E., and Anderson, I. M.: Profound Hypothermia in Cardiac Surgery, Lancet 1: 748, 1959.
7. Helmsworth, J. A., Shabetai, R., Cole, W. R., Neely, J. C., Albers, J. E., and Gonzales, L. L.: A Method of Cardiac By-Pass With Autogenous Oxygenation, Surgery 45: 129, 1959.
8. Lewis, F. J., Horwitz, S., and Naines, J.: Semi-Automatic Blood Pump for Cardiac By-Pass. (To be published.)
9. Mustard, W. T., Sapirstein, W., and Pay, D.: Cardiac Bypass Without Artificial Oxygenation, J. THORACIC SURG. 36: 479, 1958.

10. Potts, W. J., Riker, W. L., DeBord, R., and Andrews, C. E.: Maintenance of Life by Homologous Lung and Mechanical Circulation, Surgery 31: 161, 1952.
11. Read, R. C., George, V. P., Cohen, M., and Lillehei, C. W.: Cardiac By-Pass Using Autogenous Lung for Oxygenation, Surgery 40: 840, 1956.
12. Shields, T. W., and Lewis, F. J.: Rapid Cooling and Surgery at Temperatures Below 20° C., Surgery 46: 164, 1959.
13. Sirak, H. D., Ellison, E. H., and Zollinger, R. M.: Cardiotomy Into an Empty Left Ventricle, Surgery 28: 225, 1950.
14. Wesolowski, S. A., and Welch, C. S.: Experimental Maintenance of Circulation by Mechanical Pumps, Surgery 31: 769, 1952.

THE USE OF SILICONE IN MAINTAINING PATENCY IN DRAINAGE TUBES

George A. Harkins, M.D., San Francisco, Calif.*

IT HAS BEEN FOUND that blockage due to blood clot formation within chest drainage tubes has been avoided to a large extent by pretreatment of these tubes with silicone. Since adopting this measure 2 years ago, it has become unnecessary to milk the tubes frequently in order to maintain patency, and drainage failure in such catheters is a rarity. We have been unable to detect any harmful effect from the use of silicone for this purpose and believe it has added to the ease and safety of postoperative care.

The application of silicone is a simple matter and can be carried out with a large number of tubes simultaneously. In this hospital, the rubber tubes are washed, dipped into a bath of 5 per cent Silicone,† rinsed in distilled water, and baked in the oven until dry (10 to 20 minutes at 160° C.). Thereafter they are sterilized and used as necessary.

Pleural catheters siliconized in this manner have been used in more than 500 patients, and we can recommend the general adoption of this practice in thoracic surgery. In addition, pretreatment with silicone might afford better drainage in catheters placed following other operations, for example, after prostatectomy, radical neck dissection, and radical mastectomy.

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*Present address: The Children's Medical Center, Boston, Massachusetts.

†Silicone, Z4141—Dow Corning Corp., Midland, Michigan.

CONSTITUTION OF THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

As Amended to May 12, 1960

Article I. Name

SECTION 1.—This Association shall be known as the American Ass for Thoracic Surgery.

Article II. Object

SECTION 1.—The object of the Association shall be to encourage and late investigation and study that will increase the knowledge of intrat physiology, pathology, and therapy, to correlate such knowledge an seminate it.

SECTION 2.—To attain this object, the Association shall hold at lea scientific meeting every year in which free discussion shall be featured: conduct a Journal for the publication of the papers presented at this me and other acceptable articles; and shall undertake such other activities Council or the Association as a whole may decide.

Article III. Membership

SECTION 1.—There shall be four classes of members: Active, Asso Senior, and Honorary. Admission to membership in the Association shall election. Membership shall be limited, the limits on the respective c to be determined by the By-Laws. Only Active and Senior Members shall the privilege of voting or holding elective office.

SECTION 2.—Election to Active, Senior, and Honorary Membership sha for life, subject to the provisions of Section 3, following. After the Annual Meeting of the Association, election to Associate Membership sha for a limited period of time, as determined by the By-Laws. During this lim period, an Associate Member, if properly qualified, may be elected to Ac Membership. At the expiration of this limited period, an Associate Mem if not yet qualified for Active Membership, must either be reelected to an ditional period of Associate Membership, or be dropped from the rolls of Association.

SECTION 3.—Membership may be voluntarily terminated at any time members in good standing. The Council, acting as a *Board of Censors*, m recommend the expulsion of a member on the grounds of moral or profession delinquency, and submit his name, together with the grounds of complaint, to the Association as a whole at any of the regularly convened meetings, after giving the member so accused ample opportunity to appear in his own behalf.

ARTICLE IV. OFFICERS AND GOVERNMENT

SECTION 1.—The officers of the Association shall be a President, a Vice-President, a Secretary, a Treasurer, an Editor, and five Councilors. These ten officers and councilors shall be the governing body of the Association, and shall have full power to act on all matters, except as follows:

1. They may not alter the initiation fees or annual dues, nor levy any general assessments against the membership, except that they may, in individual cases, remit annual dues or assessments.
2. They may in no wise change the Constitution or By-Laws.
3. They may neither elect new members nor alter the status of existing members, other than to apply the provisions of Article III, Section 3.
4. They may not deplete the principal of the Endowment Fund.

SECTION 2.—Officers and Councilors shall be elected at the annual meeting of the Association, and shall take office upon conclusion of the meeting. The President and the Vice-President shall be elected for a one-year term of office and neither may be re-elected to succeed himself in the same office. The Secretary, the Treasurer, and the Editor shall be elected for a one-year term of office, and any or all may be re-elected indefinitely. The outgoing President shall automatically become a Councilor for a one-year term of office. The other four Councilors shall be elected, one each year, for a four-year term of office, but no Councilor may be re-elected to succeed himself.

SECTION 3.—Vacancies occurring among the officers and councilors during the year shall be temporarily filled by action of the Council, subject to approval of the Association at the next regularly convened meeting.

ARTICLE V. COMMITTEES

SECTION 1.—At the opening session of the annual meeting there shall be elected, after nomination from the floor of the Association, a Nominating Committee of three. This Committee shall prepare a slate of nominees for officers and councilors and shall present their report at the executive session of the Association.

SECTION 2.—The Council is empowered to appoint a Membership Committee, an Auditing Committee, a Program Committee, a Necrology Committee, and such other committees as may in its opinion be necessary. All such committees shall render their report at the executive session of the Association.

SECTION 3.—The Editor is empowered to appoint an Editorial Board, subject only to the approval of the Council.

SECTION 4.—The Association as a whole may authorize the Council to appoint Scientific or Research Committees for the purpose of investigating thoracic problems and may further authorize the Council to support financially such committees to a limited degree. In appointing such committees, the Council shall be governed by the provisions of the By-Laws.

ARTICLE VI. FINANCES

SECTION 1.—The fiscal year of the Association shall run from the beginning of one annual meeting to the beginning of the next annual meeting. The books of the Association shall be kept and audited on this basis.

SECTION 2.—Members shall contribute to the financial maintenance of the Association through the medium of initiation fees, annual dues, and special assessments. The amount of the annual dues and the initiation fees shall be determined by the By-Laws.

If, at the end of any fiscal year, there be a deficit in the current funds of the Association, the Council may send out notices to that effect and invite Active members to contribute the necessary amount so that no deficit be carried over from one fiscal year to another. The Association may, in any regularly convened meeting, vote a special assessment for any purpose consistent with the objects of the Association (Article II), and such special assessment shall become an obligatory charge against the classes of members affected thereby.

SECTION 3.—To meet the current expenses of the Association, there shall be available all revenue derived from annual dues, special assessments, and income from Endowment Fund, subject to the provisions of Section 4, following. Funds derived from the payment of initiation fees shall not be available for current expenses.

SECTION 4.—All funds derived from the payment of initiation fees shall be placed in a special fund, to be invested and reinvested in legal securities, to be held intact, and to be known as the Endowment Fund. The Council is responsible for the proper management of the Endowment Fund, and may divert any surplus in the current funds of the Association into this fund, but may not withdraw any of the principal of the Endowment Fund except in accordance with the provisions of Section 6, following.

SECTION 5.—The income from the Endowment Fund shall be expended as the Council directs.

SECTION 6.—The principal of the Endowment Fund may be withdrawn, in whole or in part, under the following conditions only: The amount of principal to be withdrawn shall have been approved by the Council; it shall have been approved by a majority of the members present and voting at a regularly convened annual meeting; it shall have been tabled for one year; it shall have been finally passed by a three-fourths vote of the members present and voting at the next regularly convened annual meeting.

SECTION 7.—In the event of the dissolution of the Association, the Endowment Fund shall be distributed among national institutions of the United States and Canada in a proportion equal to the then existing ratio between the numbers of citizens of the two nations who are members of the Association.

ARTICLE VII. MEETINGS

SECTION 1.—The time, place, duration, and procedure of the annual meeting of the Association shall be determined by the Council, and the provisions of the By-Laws.

SECTION 2.—A special meeting of the Association may be called on one month's notice on the written request of fifteen members. The specific purposes of the meeting must be stated in the request and in the official call for the meeting.

SECTION 3.—The annual meeting of the Council shall be held at or near the close of the fiscal year.

ARTICLE VIII. AMENDMENTS

SECTION 1.—This Constitution shall in no wise be changed except by a three-fourths vote of the members present at an annual meeting, and further provided that the proposed alteration or amendment shall have been moved and seconded at a previous annual meeting, and that printed copies of the suggested alteration or amendment shall have been circulated among the members, and that the members shall have been specifically advised that such alteration or amendment will be voted upon.

BY-LAWS

ARTICLE I.

SECTION 1.—These By-Laws shall merely interpret the Constitution and specifically apply its principles. They shall set forth no principles not included in the Constitution.

ARTICLE II.

SECTION 1.—All papers read before the Association shall become the property of the Association. Authors shall leave original copies of their manuscripts with the Editor or Reporter, at the time of presentation, for publication in the official journal.

SECTION 2.—When the number of papers makes it desirable, the Council may require authors to present their papers in abstract, and may set a time limit on discussions.

SECTION 3.—Members are urged to cooperate with all Scientific Committees of the Association.

SECTION 4.—Attendance at Annual Meetings and participation in the scientific programs shall be optional for all Honorary and Senior Members, but it shall be expected from all Active and Associate Members.

SECTION 5.—While the scientific session of the annual meeting is held primarily for the benefit of the members of the Association, it may be thrown open to nonmembers who are able to submit satisfactory credentials, who register in a specified manner, and who pay such registration fee as may be determined and published by the Council from year to year.

ARTICLE III.

SECTION 1.—Candidates for membership in this Association must be formally nominated and seconded, in an approved manner, by not less than three Active or Senior Members. Such nomination must have been in the hands of the Membership Committee for not less than four months, and the name of the candidate must have been distributed to the Association as a whole before final action may be taken on any new candidate for election to Active or Associate Membership. Provided the foregoing requirements have been met, and the candidates have been approved by the Membership Committee and by the Council, their names shall be presented to the Association at a regularly convened annual meeting for final action. A three-fourths vote of those present and voting shall be required to elect. Any candidate for membership in this Association who has failed of election for two successive years shall automatically cease to be a candidate and may not be renominated until after a lapse of three years.

SECTION 2.—Active Membership shall be limited to three hundred fifty. The candidate, to be eligible, must be a citizen of the United States of America or of Canada, unless in unusual cases this citizenship requirement shall have been waived by the Council. The candidate shall have achieved distinction in the thoracic field, or shall have made a meritorious contribution to knowledge pertaining to thoracic disease or its surgical treatment. Under usual circumstances, Active Members shall be elected from the Associate Members who have satisfied all requirements for Active Membership. Under unusual circumstances, Active Membership may be awarded to new candidates of outstanding distinction.

SECTION 3.—There shall be no numerical limit on Associate Membership. The candidate, to be eligible, may be a citizen of any country. All candidates for Associate Membership shall be engaged actively in the practice of clinical medicine, or in teaching, or investigative work in the basic sciences underlying clinical practice, and all shall have demonstrated an active interest in thoracic disease. In the case of those who are engaged in the independent practice of thoracic surgery, it shall be required that they present evidence of sound basic training in general as well as thoracic surgery. Clinicians of outstanding ability, whose interest is limited to a small fraction of the entire thoracic field, may be elected to Associate Membership. The limited period of time for Associate Membership as required by Article III, Section 2, of the Constitution, shall be five years.

SECTION 4.—The number of Senior Members shall be unlimited. The candidate, to be eligible, must have been an Active Member of the Association for not less than ten years or, having been an Active Member, have passed the age of sixty years, or become incapacitated by illness.

SECTION 5.—Honorary Membership shall be reserved for such distinguished persons as may be deemed worthy of this honor by the Council with concurrence of the Association.

SECTION 6.—The report of the Membership Committee shall be rendered at the annual Executive Session of the Association. Candidates shall be presented in groups in the following order: Candidates for Honorary Membership; retirement of Active Members to Senior Membership; candidates for Active Membership; candidates for Associate Membership.

SECTION 7.—The Council shall recommend that any Active or Associate Member whose dues are in arrears for two years, or who has been absent, without sufficient excuse, from three consecutive annual meetings, shall have his membership terminated.

SECTION 8.—Notwithstanding Section 7, any member of the Association over 60 years of age is excused from the attendance requirement and upon his specific request may likewise be excused from the payment of dues.

ARTICLE IV.

SECTION 1.—The President of the Association shall perform all duties customarily pertaining to the office of President. He shall not only preside at all meetings of the Association, but also at all meetings of the Council. The President shall be elected from the Active Members of the Association.

SECTION 2.—The Vice-President of the Association shall perform all duties customarily pertaining to the office of the Vice-President, not only as to the Association, but also as to the Council. The Vice-President shall be elected from the Active Members of the Association.

SECTION 3.—The Secretary of the Association shall perform all duties customarily pertaining to the office of Secretary. He shall serve not only as Secretary of the Association but also as Secretary of the Council. The Secretary shall be elected from the Active Members of the Association.

SECTION 4.—The Treasurer of the Association shall perform all duties pertaining to the office of Treasurer. He shall not only serve as Treasurer of the Association but shall also serve as custodian of the Endowment Fund. The Treasurer shall be elected from the Active Members of the Association.

SECTION 5.—The Editor of the Association shall be the Editor of the official Journal and shall, ex officio, be the Chairman of the Editorial Board. The Editor shall be elected from the Honorary, Active, or Senior Members of the Association.

SECTION 6.—The Councilors of the Association shall hold office as specified in the Constitution. They shall be elected from the Active or Senior Members of the Association.

SECTION 7.—In the event of a vacancy occurring in the office of President, the Council shall advance the Vice-President to the Presidency and appoint a new Vice-President under the Provisions of Article IV, Section 3, of the Constitution.

ARTICLE V.

SECTION 1.—The Nominating Committee shall consist of three Active or Senior Members who are, by preference, also past Presidents of the Association and in attendance at the meeting. They shall be elected in accordance with the provisions of Article V, Section 1, of the Constitution. The Council shall instruct the Committee as to the vacancies which are to be filled by election.

SECTION 2.—The Membership Committee shall consist of seven Active or Senior Members appointed in accordance with the provisions of Article V, Section 2, of the Constitution. The Council may appoint not more than one of its own members to serve on this Committee. The duties of the Membership Committee are to investigate all candidates for membership in the Association and to report their findings as expeditiously as possible to the Council through the Secretary of the Association. This Committee is also charged with searching the literature of this and other countries to the end that proper candidates may be presented to the Association for consideration. Appointment to this Committee shall be for a period of one year, and not more than five of the members may be reappointed to succeed themselves. This Committee is also charged with maintaining a record of membership attendance and participation in the scientific programs and reporting to the affected members and to the Council any deviations from the requirement of Article II, Section 4, of these By-Laws.

SECTION 3.—The Auditing Committee shall consist of three Active or Senior Members appointed in accordance with the provisions of Article V, Section 2, of the Constitution. None of these may be selected from the officers or councilors of the Association. Their duty shall be to audit the accounts of the Association at the end of each fiscal year and render their report to the Council of the Association through the Secretary. Appointments to this Committee shall be made for a one-year term. Not more than two members may be reappointed to succeed themselves.

SECTION 4.—The Program Committee shall consist of five members: The President of the Association, the Secretary of the Association, the Editor of the Association, and two members at large, one of whom shall be resident at or near the place of annual meeting. The duties of this Committee shall be to arrange, in conformity with instructions from the Council, the scientific program for the annual meeting.

SECTION 5.—The Necrology Committee shall consist of one or more Active or Senior Members, and shall be appointed in accordance with the provisions of Article V, Section 2, of the Constitution. Appointments to this Committee shall be for a one-year term of office. Any or all members of this Committee may be reappointed to succeed themselves. The Council may, if it so desires, appoint one of its own members to serve as Chairman of this Committee. The duties of the Necrology Committee shall be to prepare suitable resolutions and memorials upon the deaths of all members of the Association and to report such deaths at every annual meeting.

SECTION 6.—The Editorial Board shall be appointed by the Editor, subject only to the approval of the Council. The Editor shall be, ex officio, the chairman of this board and shall be privileged to appoint and indefinitely reappoint such members of the Association, regardless of class of membership, and such nonmembers of the Association as in his opinion may be best calculated to meet the editorial requirements of the Association.

SECTION 7.—When Scientific or Research Committees are authorized by the Association, the Council shall appoint the Chairmen of these Committees, with power to organize their committees in any way best calculated to accomplish the desired object, subject only to the approval of the Council. Financial aid rendered to such Committees shall not exceed such annual or special appropriations as may be specifically voted for such purposes by the Association as a whole.

ARTICLE VI.

SECTION 1.—Honorary Members of the Association are exempt from all initiation fees, dues, and assessments.

SECTION 2.—Annual dues for Active Members shall be $30.00.

SECTION 3.—Annual dues for Associate Members shall be $25.00.

SECTION 4.—Senior Members are exempt from dues.

SECTION 5.—Initiation fee for those elected directly to Active Membership shall be $15.00.

SECTION 6.—Initiation fee for those elected to Associate Membership shall be $10.00. If and when an Associate Member is elected to Active Membership, he shall pay an additional $5.00 initiation fee.

SECTION 7.—Income from the Endowment Fund shall be expended as the Council directs.

SECTION 8.—Associate and Active Members must subscribe to THE JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY to retain their membership status.

SECTION 9.—Senior Members may retain their membership status without the payment of annual dues and subscription to THE JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY is optional.

(Note.—Bills for membership dues and for subscriptions to THE JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY will be mailed to members by the Treasurer after the Annual Meeting.)

ARTICLE VII.

SECTION 1.—When the Association convenes for its annual meeting, it shall immediately go into executive session, but the business at this session shall be limited to:

1. Election of Nominating Committee.
2. Appointment of necessary committees.
3. Miscellaneous business of an urgent nature.

SECTION 2.—The annual executive session of the Association shall be held at the opening of the afternoon session of the second day of the meeting. The order of business shall be:

1. Reading of the minutes of the preceding meetings of the Association and Council.
2. Report of the Treasurer for the last fiscal year.
3. Report of the Auditing Committee.
4. Report of the Treasurer for the current year to date.
5. Report of the Necrology Committee.

6. Report of the Program Committee.
7. Action on amendments to the Constitution and By-Laws.
8. Action on recommendations emanating from the Council.
9. Unfinished Business.
10. New Business.
11. Report of the Membership Committee.
12. Election of new members.
13. Report of the Nominating Committee.
14. Election of officers.

SECTION 3.—At the annual meeting of the Council the order of business shall be:

1. Reading of minutes.
2. Treasurer's report.
3. Appointment of committees.
4. Determination of instructions to be given to Auditing, Membership, Necrology, and other committees except Program Committee.
5. Determination of details in connection with the annual meeting.
6. Appointment and instructions to the Program Committee.
7. Unfinished Business.
8. New Business.

SECTION 4.—There shall be an annual meeting of the Council.

ARTICLE VIII.

SECTION 1.—These By-Laws shall in no wise be changed except by a two-thirds vote of the members present at the annual meeting or a properly convened meeting of the Association, and further provided that the proposed action or amendment shall have been moved and seconded by not less than three of the members in a properly convened annual or special meeting of the Association.

SECTION 2.—These By-Laws may be suspended in whole or in part for a period of not more than twelve hours by a unanimous vote of those present at any regularly convened meeting of the Association.

Announcements

THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

Notice of Annual Meeting

The Forty-first Annual Meeting of The American Association for Thoracic Surgery will be held April 24, 25, and 26, 1961, in Philadelphia, Pennsylvania. Headquarters will be the Sheraton Hotel.

Requests for Hotel Reservations

These should be mailed directly to Mr. Brian Kirby, Reservation Manager, Sheraton Hotel, Philadelphia 3, Pennsylvania. Please mention this Association, the type of accommodation desired, the date, and approximate hour of arrival and departure. If accommodations are desired elsewhere please communicate directly with the hotel of your choice.

Material for the Program

Scientific Papers.—Abstracts of all papers proposed for presentation at the 1961 meeting *must be received on or before* November 15, 1960, otherwise they will not be considered by the Program Committee. These should be labeled "For Thoracic Surgery Forum" or "For Regular Program" depending upon the nature of the subject matter, in the same manner as in previous years. They should contain from 200 to 250 words that accurately reflect the content of the completed paper.

Six, repeat, six clearly legible copies of *each* abstract must be sent to Miss Ada Hanvey, Administrative Assistant, The American Association for Thoracic Surgery, 308 Carondelet Building, 7730 Carondelet Avenue, St. Louis (Clayton) 5, Missouri.

Essayists selected for the program are reminded that papers presented at the meeting *must* be handed to the secretary *immediately* after their presentation. If they are not ready at that time there is a chance that they will not be published in The Journal of Thoracic and Cardiovascular Surgery.

Applications for Membership

Applications for Associate Membership in the Association must be received by the Membership Committee *not later than* **November 15, 1960,** otherwise the application will be deferred for consideration until the 1962 meeting.

Applicants must be sponsored by three Active or Senior Members of the Association. In addition to the signature on the application form, the sponsors will forward a *separate* letter concerning the applicant directly to:

Frank Gerbode, M.D.
Chairman of the Membership Committee
Presbyterian Medical Center
San Francisco 15, California

Sponsors are reminded that *new* letters of recommendation must be forwarded to the Chairman of the Membership Committee should their applicants be held over for reconsideration a *second year.*

The Journal of
Thoracic and
Cardiovascular Surgery

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Original Communications

THE SUBCORONARY IMPLANTATION OF A FLEXIBLE TRICUSPID AORTIC VALVE PROSTHESIS

Benson B. Roe, M.D., Mervyn F. Burke, M.D. (by invitation), and Harry Zehner, Jr., M.D. (by invitation), San Francisco, Calif.

TWO YEARS AGO we reported to this Association that a flexible plastic tricuspid aortic valve prosthesis had undergone successful testing in animals by long-term implantation in the ascending aorta.[1-4] Three dogs in which these valves have been implanted are still living and angiograms have shown the prosthetic valve to be still competent. When the anatomic valve was made incompetent in these animals they did not survive. It was evident that the subcoronary position of the valve was necessary for coronary filling during diastole and that the usefulness of this valve would be dependent upon the development of a technique for placing it there.

Several improvements in the design, material, and production of this valve have since been effected. While maintaining the basic characteristics of the cusps, we have incorporated new features which have made the valve suitable for intracardiac implantation in the subcoronary position. The current model (Fig. 1) is constructed so that it has the shortest possible axial length which is still adequate to support the valve cusps. Since the septal leaflet of the mitral valve forms the medial wall of the left ventricular outflow tract (see Fig. 5, *A*), it is essential that the prosthesis not protrude into the ventricle. Obviously the distal edge of the prosthesis must be proximal to the ostia of the coronary arteries. Unfortunately the distance between these two structures is only a

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few millimeters and provides the greatest limiting factor to prosthetic implantation. Additional shortening of the valve jacket in the critical area beneath the coronary ostia has been accomplished by scalloping the distal edge (Fig. 1).

Since the elastomer (silicone) material of which this valve is constructed has proved to be resistant to clotting and tissue reaction, its fixation was dependent upon sutures and friction in the formerly reported technique. In the *subcoronary position, however, the valve will not be held by the surrounding* tissues because of the irregularly tapering contour of the outflow tract (Fig. 2) and the proximity of the highly flexible mitral valve leaflet. For this reason it has been essential to incorporate two additional features in the jacket: (1) a ring of silicone rubber with greater hardness through which sutures are less likely to tear, and (2) a ring of Ivalon sponge bonded to the silicone which we *hope will be invaded by fibrous* tissue for fixation if the sutures fail to hold (Fig. 3).

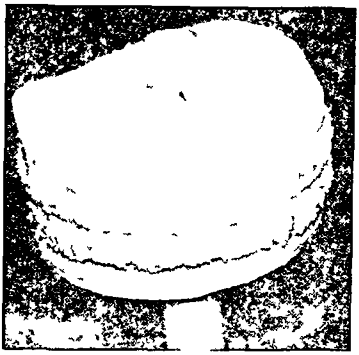

Fig. 1.—Photograph of the smooth-surfaced flexible valve. A single cusp is retracted in the open position. Note the cut-away in the cylinder between the commissures which provides a margin for the coronary ostia. Note also the compressed Ivalon ring which has protected contact with the endothelium.

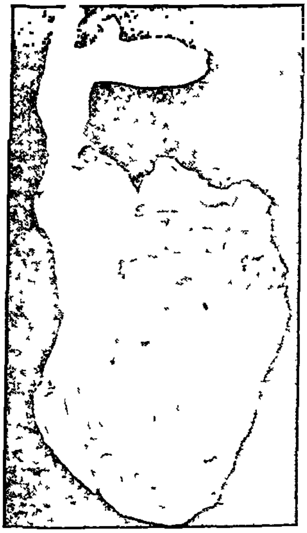

Fig. 2.—Plaster casting of left ventricular outflow tract and aorta in a dog. Note that there is no ring in the valve area.

TECHNIQUE OF IMPLANTATION

Technical difficulties were encountered in our initial attempts to suture this valve into place precisely in the area described so that neither the coronary ostia nor the mitral valve was obstructed. Surgical exposure of the full circumference of the aortic "root" is limited and awkward at best, particularly through a vertical aortotomy. The placing of sutures was nearly impossible by ordinary methods because of the difficulty in directing needles vertically. The present technique, however, has largely overcome these obstacles and it is now possible to insert the valve in the subcoronary position through a transverse aortotomy (Fig 4) with seven precisely placed sutures in a period which seldom exceeds 30 minutes of aortic cross-clamping. Myocardial ischemia is reduced

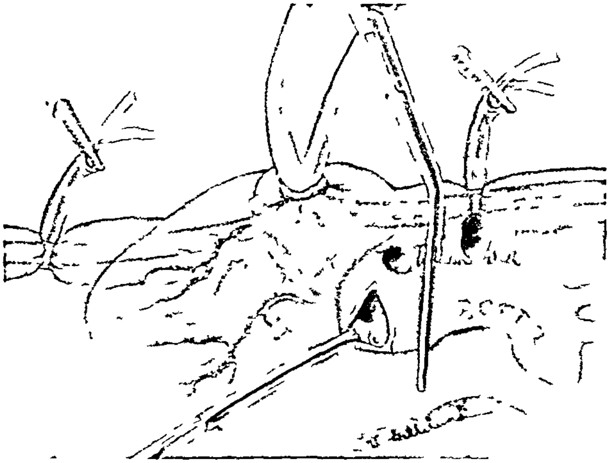

Fig 3—Diagram of sagittal section through valve prosthesis which shows position of suture, location of hard plastic band, and Ivalon sponge "jacket" Note flared edges for tight surface contact.

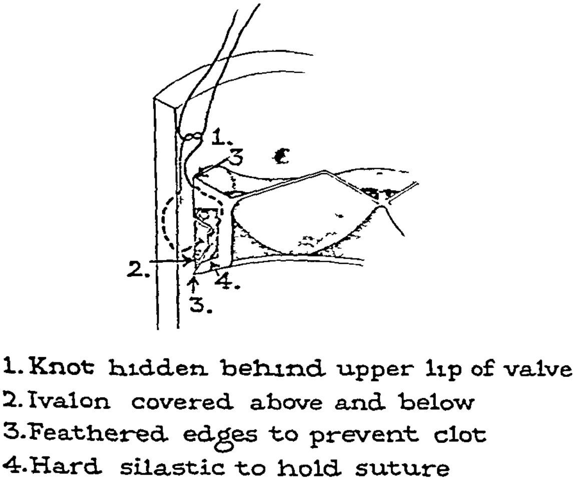
1.
3
2.
4.
3.
1. Knot hidden behind upper lip of valve
2. Ivalon covered above and below
3. Feathered edges to prevent clot
4. Hard silastic to hold suture

Fig 4—Diagram of operative approach through a right thoracotomy.

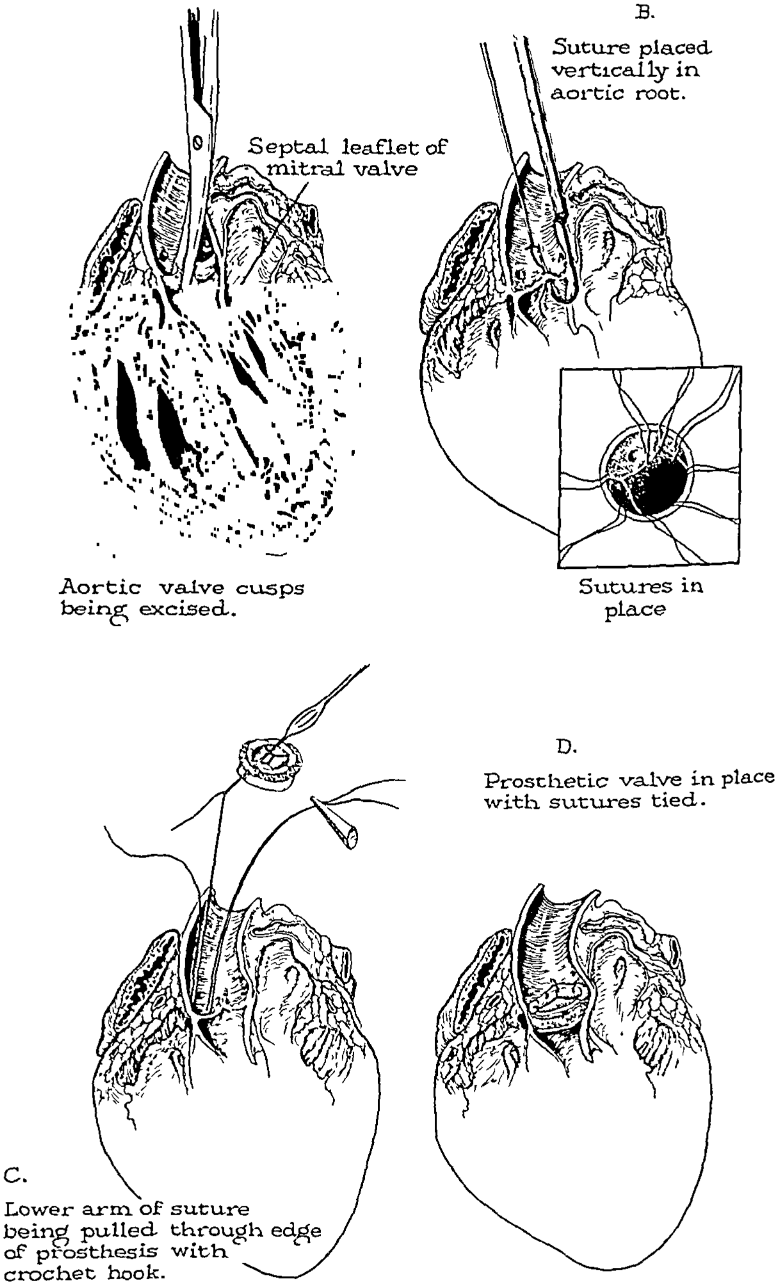
B.
Suture placed vertically in aortic root.
Septal leaflet of mitral valve
Aortic valve cusps being excised.
Sutures in place
D.
Prosthetic valve in place with sutures tied.
C.
Lower arm of suture being pulled through edge of prosthesis with crochet hook.

Fig. 5.—Diagrams of suturing technique.

A, Resection of remaining anatomic cusps.

B, Introduction of "J" needle from below upward through the valve remnant. The free end of the suture is drawn through the tissue and fed out from a spool through the hollow needle. The needle is then withdrawn to deliver the lower arm of the suture.

C, The crochet hook is inserted through the edge of the prosthetic valve and draws the bottom arm of the suture through the plastic material.

D, Prosthetic valve in place with sutures tied.

by producing regional (cardiac) deep hypothermia and by additional intermittent perfusion of the coronary ostia with cold blood during the procedure.

To permit accurate placing of sutures it is necessary to excise the anatomic cusps of the diseased valve (or the normal cusps of the valve in the experimental animal) (Fig. 5, *A*). The sutures necessary for holding the valve to the aortic wall must be placed in an axial direction parallel to each other and at the same level below the coronary ostia. This maneuver is accomplished under direct vision with a specially developed hollow "*J*" needle which has been described elsewhere[5] (Fig. 5, *B*). One suture is placed in each of the three commissures and one or more sutures in each cusp remnant, according to the size of the valve.

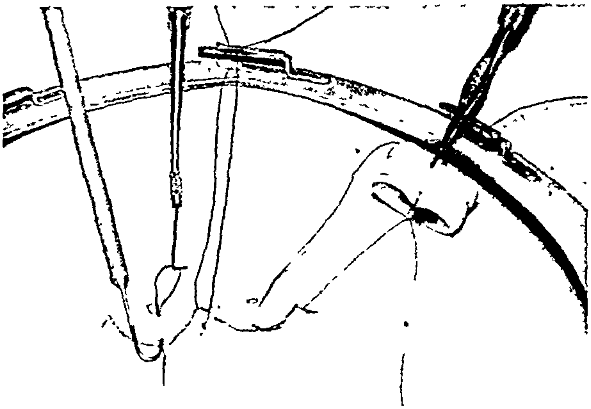

Fig. 6.—Suture technique demonstrated with instruments and simulated valve. Note superimposed clips to maintain sutures in alignment on the flat metal ring which surrounds the operative field.

To prevent tangling, the multiple suture ends are held in clips on a metal ring which surrounds the operative field (Fig. 6). Twisting is also avoided and the lower limb of the suture is quickly identified in the top clip when the suture is later passed through the prosthesis.

After all the sutures have been placed in the aortic wall, a crochet hook is used to draw the lower limb of each suture through the wall of the prosthetic valve around the hardened ring in an appropriate position on the prosthetic cuff to match the location of the suture on the aortic wall (Fig. 5, *C*). This step is accomplished in such a way that the suture holes and knots are covered behind the valve jacket. The valve is then slid down the sutures into position and the sutures are tied (Fig. 5, *D*). The aortotomy is then closed.

RESULTS

In early attempts to implant a prosthesis in the subcoronary location, the incidence of technical failure was high but several animals survived long enough to demonstrate that the valve worked. Since the development of the technique described, we have operated on 21 animals with extracorporeal circulation and cardiac arrest with regional hypothermia. In every instance the prosthetic valve was implanted satisfactorily. All but one heart developed ventricular fibrillation on rewarming but one or two defibrillatory shocks resulted in regular effective contractile beat in every animal. In 4 dogs the hearts returned to persistent ventricular fibrillation as the result of unexplained myocardial infarcts developed during the procedure. Three dogs died of uncontrolled bleeding from the aorta when normal circulation had been restored.

The remaining 14 dogs maintained satisfactory vital signs, temporarily supported by vasopressors, for an average period of 8 hours. Their chest incisions were closed, heparinization was neutralized, and spontaneous breathing restored. Death occurred from 2 to 18 hours later, usually with a gradually declining blood pressure or evidence of neurological damage.

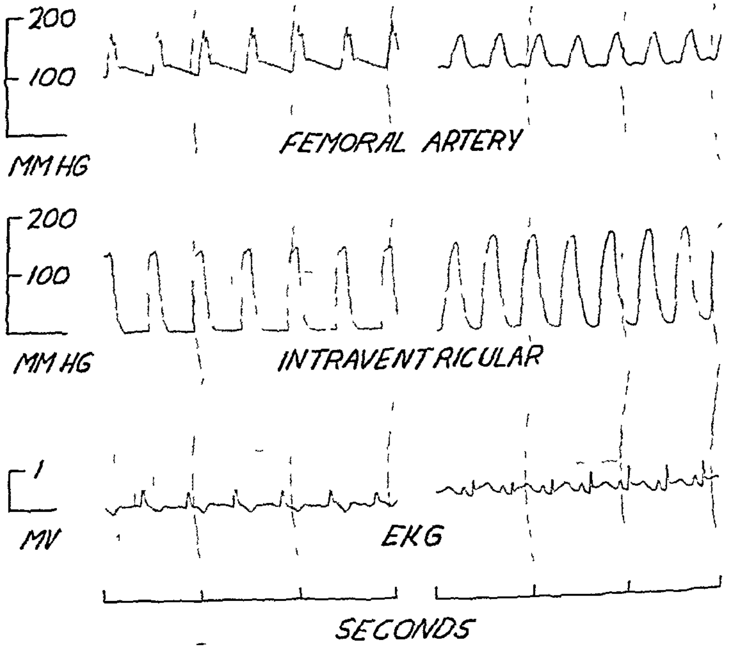

Fig 7.—Simultaneous pressure curves of normally beating heart above and below prosthetic aortic valve. (Preoperative pressures on the *left* and postoperative on the *right*.) Note dicrotic notch and absence of systolic gradient.

Pressure determinations after implantations (Fig. 7) reveal no systolic gradient across the valve, a dicrotic notch, and a normal systemic diastolic pressure with a zero intraventricular pressure. This evidence supports the observation of valve function in a pulse duplicator which shows complete competence.

Unfortunately, we have not yet been successful in maintaining long-term survivors to determine the eventual fate of this prosthetic valve, but the clinical course and the physiologic data on these animals suggest that death was the result of either prolonged cardiac ischemia or was due to our extracorporeal perfusion technique, rather than to the presence of the prosthesis in the heart.

Autopsy examinations have revealed no evidence of obstruction to the coronary ostia in this series. There has been no clot formation on the valve and no avulsion of sutures. Small to moderate-sized hematomas have been found in the subserosal layer of the mitral valve leaflet and in the interatrial septum. Large hematomas were sometimes found also in the periaortic fat pad and in the atrioventricular groove. The occurrence of all these hematomas appears to be related more to the aortotomy closure than to valve placement since they also appeared in the hearts of animals subjected to control procedures without valve implantation.

SUMMARY

A technique has been described for implantation of a short flexible aortic valve prosthesis in the subcoronary position under direct vision in the experimental animal. It has been shown that normal hemodynamics can be restored by this procedure after total ablation of the anatomic valve. Coronary blood flow is not obstructed. Previous long-term studies indicate that the physical characteristics of the valve satisfactorily prevent clotting and maintain function. Long-term survivors are still needed to determine whether permanent fixation can be expected from this technique.

REFERENCES

1. Roe, B. B., Owsley, J. W., and Boudoures, P. C.: Experimental Results With a Prosthetic Aortic Valve, J. THORACIC SURG. 36: 563-570, 1958.
2. Roe, B. B., and Moore, D.: Design and Fabrication of Prosthetic Valves, Exper. Med. & Surg. 16: 177-182, 1958.
3. Roe, B. B.: A Simple Device to Facilitate Coronary Artery Perfusion, Surgery 44: 554-555, 1958.
4. Roe, B. B., Najarian, J. S., and Moore, M.: A Technic for Insertion of a Flexible Aortic Valve Prosthesis Into the Ascending Aorta, Ann. Surg. 145: 388-391, 1957.
5. Roe, B. B.: A Simplified Technique for Closure of Interventricular Septal Defects, J. THORACIC SURG. 40: 232, 1960.

(For Discussion, see page 681)

EXPERIMENTAL PRODUCTION OF AORTIC STENOSIS

Anthony J. Munoz, M.D. (by invitation), and Sam E. Stephenson, Jr., M.D. (by invitation), Nashville, Tenn.

The production of lesions simulating acquired human cardiac lesions presents a major problem in laboratory animals. Previous work directed at the production of experimental aortic stenosis has utilized the application of a cannula,[1] metal clips,[2] or sutures[3] in the commissures. These experiments have afforded unpredictable and inconstant degrees of aortic stenosis. In an attempt to produce coronary arteriosclerosis in the experimental animal it was noted that the first site of plaque formation in the animals was one encircling the aortic annulus and, in some cases, fusion of the commissures developed. This then represents the early lesion of aortic stenosis.

METHOD

Unselected mongrel male dogs, weighing from 11 to 23 kilograms, were utilized. After a baseline electrocardiogram and serum cholesterol levels were obtained, the animals were given 2 millicuries per pound of I^{131} to render the dogs euthyroid or hypothyroid. (In a second group of animals [Group B], propylthiouracil, 750 to 1,000 mg. per day, was substituted for the radioactive iodine.) After a 2-week delay the animals were started on 100,000 I.U. of vitamin D daily and placed on a special diet (Table I). Fresh meat was added at frequent intervals.

Table I*

A.	
Commercial dog meal	93 grams
Commercial lard	5 grams
Crystalline cholesterol	2 grams
B.	
Cooking oil	73.0 grams/100
Cholesterol	20.0
Cholic acid	5.0
Thiouracil	2.0

*Diet A was utilized in combination with I^{131} and diet B when thiourea derivative was substituted.

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The vitamin D was continued until the dogs demonstrated the toxic manifestations of weight loss and bleeding from the gums and it was then reduced by one half. The special diet was continued until sacrifice. Monthly serum cholesterol levels were obtained (Table II). At the time of sacrifice some animals had coronary arteriograms and others had left heart catheterization for the gradient across the aortic valve.

TABLE II*

A. I^{131}	+ Diet	+ Vitamin D
	Avg. Mg./%	*Range*
Preop.	154	125-180
1 mo.	833	450-1,120
2 mo.	965	620-1,170
3 mo.	1,094	775-1,360
B. Thiouracil	+ Diet	+ Vitamin D
	Avg. Mg./%	*Range*
Preop.	171	115-235
1 mo.	159	105-195
2 mo.	303	225-355
3 mo.	371	235-490
4 mo.	638	575-740
5 mo.	605	500-770
6 mo.	940	660-1,450

*The group A animals show the more rapid rise in serum cholesterol levels achieved with this method and the lesions were more prominent in this particular group.

The excised heart and great vessels were examined, photographed, and preserved in formalin solution. In some cases the entire heart and great vessels were stained with Sudan III for localization of fatty deposits not grossly visible. Typical areas of plaque formation were submitted for microscopic examination.

RESULTS

Six animals were prepared, using radioactive iodine, vitamin D, and the high cholesterol diet. All animals were sacrificed at 3 months and all showed marked atherosclerosis encircling the aortic annulus (Fig. 1). In some animals there were also marked changes in the pulmonary artery, arch of the aorta, descending aorta, and abdominal aorta. These areas of involvement grossly resembled human plaques, both in their appearance and location. The location of these plaques was primarily on the superior wall of the thoracic aorta, around the orifices of the branch vessels, and on the posterior wall of the abdominal aorta. Unfortunately pressure gradients were not obtained on these animals as the finding of commissure fusion was unexpected.

Four additional animals were prepared, but propylthiouracil rather than I^{131} was given to suppress thyroid function. Although these animals also responded with a high serum cholesterol level, the findings were not as consistent and plaque formation not as prominent. These animals were sacrificed at the end of 6 months and demonstrated an average gradient of 49 mm. Hg across the aortic valve.

The serum cholesterol values on these animals prepared with radioactive iodine averaged 1,094 mg. % at 3 months. It is possible, however, with this regimen to obtain cholesterol values in excess of 1,800 mg. %. In reviewing these groups of animals it seems that levels in excess of 600 to 800 mg. % need to be maintained for 3 consecutive months and then satisfactory plaque formation will have occurred.

It must be stated that the lesions observed in these animals have not progressed as yet to the full blown "pile of rocks" so classically seen in clinical calcific aortic stenosis. These lesions have been early lesions suggestive of aortic stenosis, both to us and to the pathologist. The gross lesions have appeared as deposits with or without calcification encircling the annulus, fusion of the commissures, and fatty deposition on the leaflets, the latter demonstrated by supravital staining of the gross specimen with Sudan III.

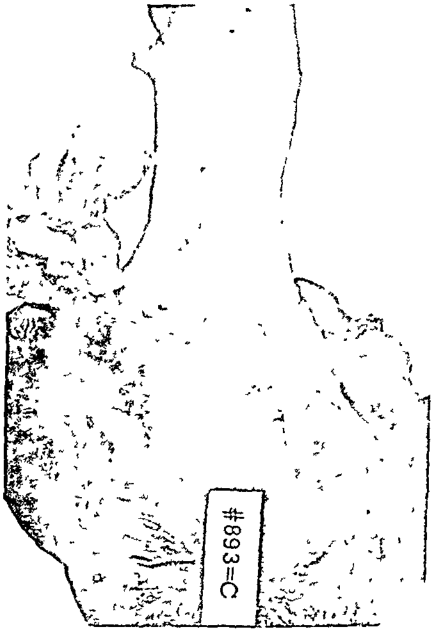

Fig. 1.—Photograph of typical specimen from animal sacrificed at 3 months. Commissure fusion is not as marked in this specimen as in some but it also demonstrates the lesions in the arch, pulmonary artery, and coronary arteries.

Attempts to demonstrate this degree of aortic stenosis by arteriographic means have not been satisfactory. Demonstration of the nicking from plaque formation in the main and branch coronary arteries has been possible by radiographic study prior to sacrifice.

Although the gross examination of these specimens resembles the plaques seen in human arteriosclerosis, the microscopic appearance is somewhat different and thus not completely analogous. We would like to reproduce the human counterpart of the disease but these experimental lesions offer a means heretofore unavailable for the study of the early changes of aortic stenosis, coronary sclerosis, and partial *occlusion (by plaque formation* and narrowing) of the small branch vessels.

The microscopic picture is primarily one of subintimal hemorrhage and fatty deposits in the early stages. These changes are soon followed by an increase in fibrous tissue, large fatty deposits, and, later, marked calcification of these areas (Fig. 2) with elevation of the intima, progressing in some cases to actual intimal ulceration. For the most part these changes are similar to the lesion in medial sclerosis.

DISCUSSION

The early work of Creech and associates[4] pointed out the feasibility of the development of arteriosclerotic-like plaques in dogs. Up until that time this lesion had been extremely difficult to produce. Soon after the reported work of Creech, we set up a long-term study, using the Tulane method of producing arteriosclerotic disease, in an attempt to assess mechanical factors concerned in the selective deposition of the material. Through a period of 3 years we have been able to produce some lesions. These, however, have not been of the magnitude expected and the long period of treatment is not only exhausting to the animal and the research group but the cost is exorbitant. It is possible, however, to produce changes in the abdominal aorta by this method and this process is enhanced by mechanical irritation of the vessels.

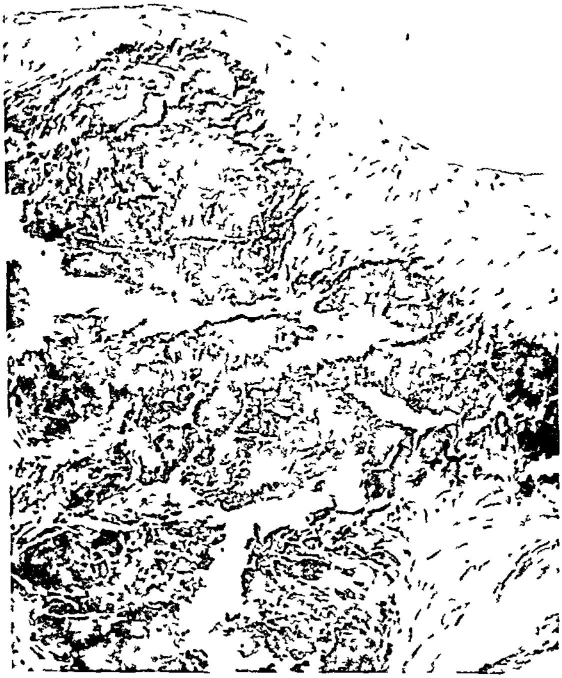

Fig 2.—Photomicrograph of lesion at the aortic annulus This animal had been treated for 90 days One can see the marked calcification and numerous cholesterol clefts (×25; reduced ⅓)

Blake,[5] using a variant of this method, was able to develop similar lesions in dogs. In these studies, coronary lesions developed in somewhat over 24 months of treatment.

Crisp[6] in 1958 reported the fairly rapid development of lesions in dogs by another method. Utilizing regular dog chow as a diet the animals were given 100,000 I.U. of vitamin D daily. After about 90 days, lesions in the media of major vessels were evident.

The procedure utilized in this report is essentially a combination of these two methods. The vitamin D in such large doses produces multiple subintimal hemorrhages. These areas of injury then predispose to the deposition of the excess lipids in these particular areas. Although the lesions produced by this method are not completely analogous to the human lesions of arteriosclerosis, the sites of deposition are the same. The experimental lesions select, in sites of decreasing frequency, the aortic annulus, the superior wall of the ascending aorta, the pulmonary artery, the lumbar portion of the abdominal aorta, and last, the coronary arteries.

It would be preferable to be able to develop lesions in animals which are microscopically the same as those in human beings. As yet this is not possible. Experiments are now in progress using primates with the same technique in an effort to evaluate this type of experimental animal. Until it is possible to develop the human type lesions, the method herein described appears to represent more closely the human counterpart than the lesions from previously described methods.

The utilization of propylthiouracil instead of radioactive iodine, for preparation of the animals before vitamin D and cholesterol are started, produces similar lesions but these lesions are not as marked, and the degree of fusion of the aortic commissures is inconstant. At the present time we consider that I^{131} should be used to produce the more marked results. It must be remembered, however, that if the animals are kept under observation for longer than 6 months, repeat treatment with I^{131} may be necessary.

It is hoped that animals prepared over a longer length of time will show a more complete and advanced aortic stenosis. Many other aspects of this over-all problem need to be evaluated and will form the basis of a subsequent report.

SUMMARY

1. A method is described to produce arteriosclerotic-like lesions in male dogs. These lesions develop in less than 90 days.

2. Among the earliest lesions are those encircling the aortic annulus and, if permitted to progress, cause fusion of the aortic commissures and the early lesions of aortic stenosis.

3. The use of I^{131}, 2 millicuries per pound of animal weight, to suppress thyroid function is superior to the utilization of antithyroid drugs for the consistent development of the lesions in this particular experiment.

REFERENCES

1. Meerson, F. Z., and Kobozev, G. W.: O methodike sozdanica eksperimentalnogo stenoza aorty, Bulletin Eksperimental'noi Biologic i meditsiny (Moskow) 39: 50-52, 1955.
2. Salemo, R. A.: The Experimental Production of Valvular Aortic Stenosis, Ann. Surg. 149: 368, 1959.
3. Boerma, J. R., Germs, J., and Blickman, J. R.: Artificial Stenosis of the Aorta, Chirurgicum Neerlandicum 3: 123, 1951.
4. Creech, O. J., Jordan, G. L., Jr., De Bakey, M. E., Overton, R. C., and Halpert, B.: The Effect of Chronic Hypercholesterolemia on Canine Aortic Transplants, Surg. Gynec. & Obst. 101: 607, 1955.
5. Blake, T. M.: Personal communication, 1960.
6. Crisp, W. W., Jr., Root, H. D., Jenson, C. B., Imamagler, K., and Yonehiro, E. G.: Experimental Production of Arteriosclerosis in the Dog, S. Forum 9: 304, 1958.

(For Discussion, see page 631)

EVALUATION OF NEW NONWETTABLE MACROPOROUS MEMBRANES WITH HIGH PERMEABILITY COEFFICIENTS FOR POSSIBLE USE IN A MEMBRANE OXYGENATOR

James S. McCaughan, M.D. (by invitation), Richard Weeder, B.A. (by invitation), John C. Schuder, Ph.D. (by invitation), and William S. Blakemore, M.D., Philadelphia, Pa.

A MEMBRANE that is permeable enough to oxygenate blood adequately without requiring a large surface area or volume of blood would be a desirable contribution in the development of a practical membrane oxygenator. Various thicknesses of different membranes have been evaluated empirically in oxygenators.[5, 7, 8, 18] Since blood must be circulated through an oxygenator and the increase in the oxygen saturation determined, these experiments have been expensive, arduous, and difficult to control.

In his experiments on the diffusion of gases through solids, Barrer[2, 4] showed that the gas first dissolves in the membrane, diffuses across the membrane, and then evaporates into the atmosphere on the other side. The permeability of the membrane is thus determined by the physical and chemical structure of the membrane and the nature of the gas diffusing through it. Except for a few anomalous systems,[12] the flow rate of a gas through the membrane can then be (1) increased linearly by increasing the partial pressure difference of the gas across the membrane, (2) decreased linearly by increasing the thickness of the membrane, and (3) increased logarithmically by increasing the absolute temperature.[1, 3, 6, 13]

From these observations, Barrer developed the concept of a permeability coefficient which is equal to the product of the solubility and diffusion constants of the gas and is defined as the standard cubic centimeters (0° C. 1 atm.) of gas passing through 1 sq. cm. of membrane (1 mm. thick) per second per centimeter of mercury partial pressure difference across the membrane.*

From the Harrison Department of Surgical Research and the Department of Surgery of the University of Pennsylvania.

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*Thus, the following mathematical expression can be derived for the flow of a gas across a polymer membrane:

$$\frac{\text{Flow rate}}{\text{Unit area}} = \frac{\text{Permeability coefficient} \times \text{Partial pressure difference}}{\text{Membrane thickness}}.$$

or

$$\frac{V}{A} = \frac{P\ (p_1 - p_2)}{t}$$

where

V = flow rate of gas across the membrane (c.c./sec.).
A = area of membrane exposed (sq. cm.).
p_1 = partial pressure of the gas on one side of the membrane (cm. Hg).
p_2 = partial pressure of the gas on the other side of the membrane (cm. Hg).
t = thickness of the membrane (mm.)
P = permeability coefficient for the given gas-membrane system at a specific temperature (c.c.-mm./cm.^{2}-cm. Hg-sec.).

By measuring the flow rate of a gas across different membranes under controlled conditions, the permeability coefficients can be calculated for those specific gas-membrane systems. From a comparison of the permeability coefficients, the most permeable membrane can then be selected.

Various experimental procedures have been used to measure these coefficients; however, they have usually been either elaborate or time consuming.[4, 5, 9, 11, 16, 18, 20, 22, 25] Although the permeability coefficients for oxygen and carbon dioxide have been determined for almost all the membranes currently available, we undertook to develop a simple technique for measuring the permeability coefficients of several new types of membranes. With this apparatus, rapid and easy preliminary studies can be performed to measure the relative permeabilities of different membranes without the necessity of using an oxygenator with all the problems it entails.

Because permeation is a solution and diffusion phenomenon, two gases will permeate different membranes with approximately the same relative rates which is dependent upon the molecular weight of a gas (Graham's law).[25] Therefore, the membranes that have the highest permeability to carbon monoxide will also have the highest permeability to oxygen. Since a sensitive carbon monoxide analyzer was available and we are interested in the permeabilities of different membranes relative to each other, we measured the carbon monoxide permeability of various standard membranes to establish a base line for future comparison. In the technique that will be described, the permeability of any gas can be determined by analyzing the gas mixtures for the specific gas with the appropriate analyzer.

PRINCIPLE

When pure carbon monoxide is passed on one side of a membrane and oxygen on the other side, some of the gases will counter diffuse through the membrane. The gas mixture leaving the oxygen side of the chamber can then be analyzed for carbon monoxide content. Since this represents the carbon monoxide that diffused through the membrane, the permeability of the membrane to carbon monoxide can be calculated (Fig. 1).

From a carbon monoxide mass balance, the perfect gas law, and the flow equation, a relationship can be derived for calculating the carbon monoxide permeability constant from the data obtained with this apparatus.*

APPARATUS

1. *Diffusion Chamber.*—This consists of two 3.5 by 3.5 by 1 in. thick hollow aluminum plates which are bolted together with a membrane secured between

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$$*P = \frac{(273)}{(T - 273)} \frac{(P_a - p_e)}{76} \left(\frac{x_e V_e t}{A(P_a + p_i)}\right)$$

where T = chamber temperature (°C)
P_a = atmospheric pressure (cm. Hg)
p_e = pressure in exhaust line from oxygen side of chamber (cm. Hg)
p_i = pressure in inflow line to CO side of chamber (cm. Hg).
V_e = flow rate of exhaust gas from oxygen side of chamber (c.c./sec.)
A = surface area of the membrane (sq. cm.)
t = membrane thickness (mm.)
x_e = mol fraction of CO in exhaust gas from oxygen side of chamber.
P = permeability coefficient for CO at temperature T (c.c.-mm./sec. cm.² cm. to STP conditions

them by 2⅛ inch diameter rubber "O" rings (*Figs. 2 and 3*). Each plate has a tube for the entrance and exit of a gas and a thermometer well. A wire screen is placed inside of each "O" ring to prevent the membrane from buckling.

2. *Manometers.*—The pressure of each entrance and exhaust gas is measured with a mercury manometer.

3. *Flowmeter.*—The flow rate of the gas in the oxygen exhaust line is measured with a 1,000 c.c. per minute capacity rotameter† and the flow rates of the carbon monoxide entrance and exhaust gases are monitored with 45 c.c. per minute capacity "Tri-Flat" flowmeters.*

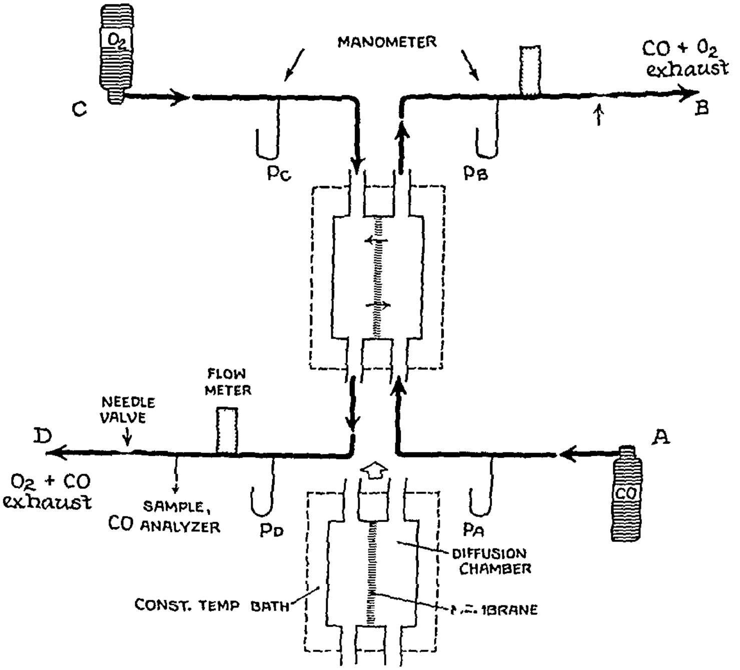

Fig. 1.—Diagram of technique used for measuring the permeability coefficients of membranes

4. *Temperature Control.*—The entire diffusion chamber is immersed in a water bath which maintained the temperature at 30 ± 0.5° C.

5. *Gas Analysis.*—The gas leaving the oxygen side of the chamber is analyzed with a Stalex† carbon monoxide analyzer for the amount of carbon monoxide present in the sample.

6. *Membrane Thickness.*—The thickness of each piece of membrane is measured with a dial micrometer.‡ This is important since there is often a size variation in the actual thickness of a membrane than that listed by the manufacturer. Also, the thickness of many of the membranes is not uniform.

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*Fisher and Porter Co., Hatboro, Pennsylvania.

†Model SI-2, Stalex Corporation, Stockholm, Sweden.

‡Model 55412, B. C. Ames Co., Waltham, Mass

PROCEDURE

After the thickness has been measured, a 7 cm. by 7 cm. piece of the membrane is placed in the diffusion chamber between the rubber "O" rings and the chamber is bolted together and immersed in the constant temperature bath.

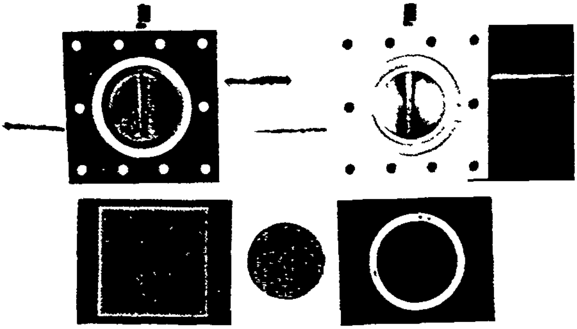

Fig 2.—Diffusion chamber disassembled

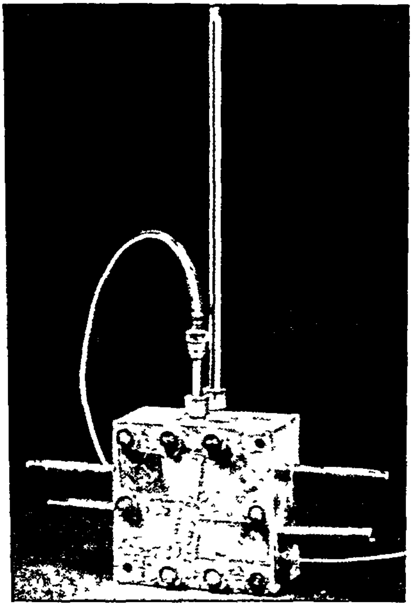

Fig 3—Diffusion chamber assembled with thermometer and thermocouple in place.

The temperature in the chamber is controlled at 30° ± 0.5° C. by a thermocouple placed in one of the thermometer wells. Oxygen is then slowly passed through one side of the chamber and carbon monoxide through the other. The needle valves on the exhaust lines are then simultaneously adjusted so the pressures on both sides of the membrane gradually rise to approximately the same value. Thus, the membrane is prevented from rupturing by keeping the total them by 2⅛ inch diameter rubber "O" rings (Figs. 2 and 3). Each plate has a tube for the entrance and exit of a gas and a thermometer well. A wire screen is placed inside of each "O" ring to prevent the membrane from buckling.

2. *Manometers.*—The pressure of each entrance and exhaust gas is measured with a mercury manometer.

3. *Flowmeter.*—The flow rate of the gas in the oxygen exhaust line is measured with a 1,000 c.c. per minute capacity rotameter† and the flow rates of the carbon monoxide entrance and exhaust gases are monitored with 45 c.c. per minute capacity "Tri-Flat" flowmeters.*

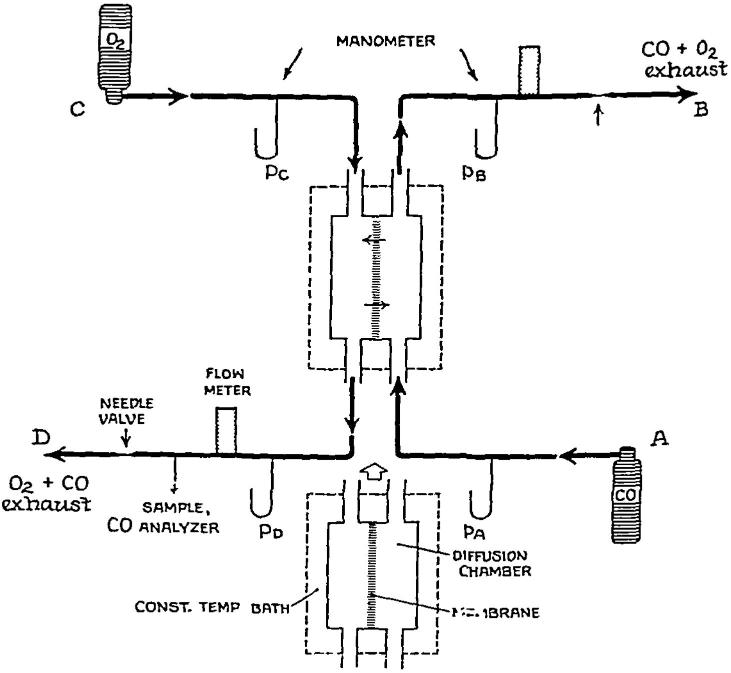

Fig. 1.—Diagram of technique used for measuring the permeability coefficients of membranes.

4. *Temperature Control.*—The entire diffusion chamber is immersed in a water bath which maintained the temperature at 30 ± 0.5° C.

5. *Gas Analysis.*—The gas leaving the oxygen side of the chamber is analyzed with a Stalex† carbon monoxide analyzer for the amount of carbon monoxide present in the sample.

6. *Membrane Thickness.*—The thickness of each piece of membrane is measured with a dial micrometer.‡ This is important since there is often a size variation in the actual thickness of a membrane than that listed by the manufacturer. Also, the thickness of many of the membranes is not uniform.

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*Fisher and Porter Co., Hatboro, Pennsylvania.
†Model Sl-2, Stalex Corporation, Stockholm, Sweden.
‡Model 55412, B. C. Ames Co., Waltham, Mass.

PROCEDURE

After the thickness has been measured, a 7 cm. by 7 cm. piece of the membrane is placed in the diffusion chamber between the rubber "O" rings and the chamber is bolted together and immersed in the constant temperature bath.

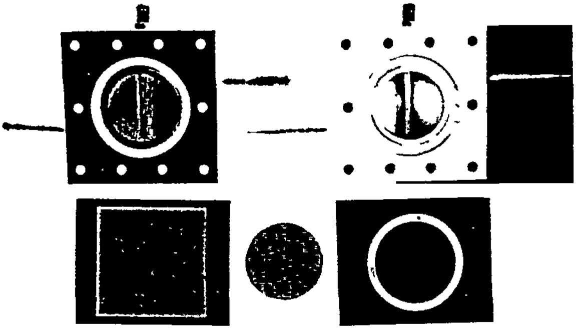

Fig 2 —Diffusion chamber disassembled

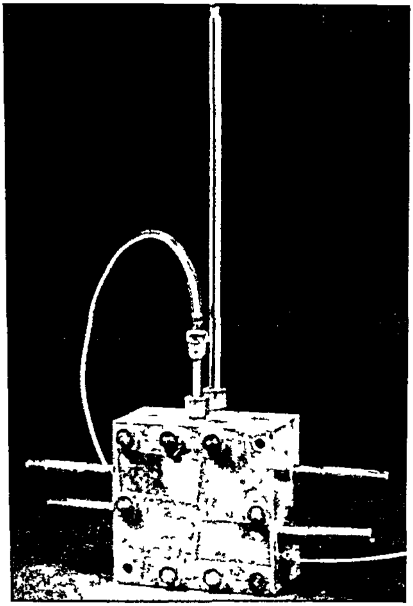

Fig 3 —Diffusion chamber assembled with thermometer and thermocouple in place.

The temperature in the chamber is controlled at 30° ± 0.5° C. by a thermocouple placed in one of the thermometer wells. Oxygen is then slowly passed through one side of the chamber and carbon monoxide through the other. The needle valves on the exhaust lines are then simultaneously adjusted so the pressures on both sides of the membrane gradually rise to approximately the same value Thus, the membrane is prevented from rupturing by keeping the total pressure gradient across the membrane negligible, although the partial pressure difference of each gas across the membrane is greater than one atmosphere.

After steady conditions have been obtained, recordings are made of the temperature of the chamber, the pressure in all of the four gas lines, and the flow rate of the gas leaving the oxygen side of the chamber. A sample of this exhaust gas is then removed with a needle and syringe and injected into the carbon monoxide analyzer which automatically records the amount of carbon monoxide present in the sample.[15] Thus, an entire experiment can be performed in less than 30 minutes.

SAMPLE DATA AND CALCULATIONS

The following data illustrate the reproducibility of the results:

Membrane: Cast Teflon	*Sample 1**	*Sample 2*	*Sample 3*
Thickness (t) (mm.)	.0127	.0063	.0127
Temperature (T) (°C.)	30.3	29.5	29.7
Pressure of oxygen exhaust (p_D) (cm. Hg)	20.0	19.5	20.0
Pressure of CO inflow (p_A) (cm. Hg)	20.0	19.5	20.0
Flow rate of oxygen exhaust (V_D) (c.c./sec.)	8.53	3.33	3.70
Surface area of membrane (A) (sq. cm.)	28.18	28.18	28.18
Mol fraction of CO in oxygen exhaust (x_D)	.000138	.000655	.000319
Atmospheric pressure (P_O (cm. Hg)	75.5	75.5	75.5
Permeability constant (c.c.-mm./sec.-cm. Hg-cm.²)	6.31×10^{-9}	5.80×10^{-9}	5.71×10^{-9}

RESULTS AND DISCUSSION

The evaluation of membranes in oxygenators has been expensive and difficult, requiring large sheets of the plastic, animals, blood, etc. These problems have been compounded by testing different thicknesses of the same membrane as though they were different membranes. By using the concept of a permeability coefficient, small pieces of experimental membranes can be tested easily. Since the permeability coefficient is expressed as though all membranes were 1 mm. thick, the necessity for testing different thicknesses of the same membrane is eliminated. However, the thickness of the membranes commercially available must be considered when making a final practical evaluation.

In using a dynamic system, such as described, to measure permeability coefficients, a minimum gas flow is required to prevent streaming and stagnation in various parts of the apparatus. This manifests itself by yielding lower and erratic diffusion rates when the flow is below the minimum value. The carbon monoxide permeability coefficients of several membranes are plotted as a function of gas flow rate in Fig. 4. Above a flow rate of approximately 100 c.c.

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*For Sample 1 the calculation was:

$$P = \frac{(273)}{(T + 273)} \left(\frac{P_O + p_D}{76}\right) \left(\frac{x_D V_D\ t}{A(P_O + p_A)}\right).$$

$$P = \frac{(273)}{(273 + 30.3)} \frac{(75.5 + 20.0)}{(76)} \frac{(.000138)\ (8.53)\ (.0127)}{(28.18)\ \ (75.5 + 20.0)}.$$

$$P = 6.31 \times 10^{-9} \frac{\text{c.c.-mm.}}{\text{sec.-cm.}^2\text{-cm. Hg}}.$$

per minute, the permeability coefficient is relatively independent of flow rate. This minimum flow rate is probably a function of the physical design of the apparatus and should be determined for each apparatus.

The permeability coefficients of several previously studied membranes were obtained for comparison with many new types of membranes which were tested. The most promising of these are E. P. Pormax,* N. P. Pormax,* and micro-polyethylene.* These "macroporous" membranes are especially prepared by mixing inert molecules, such as starch, with the plastic formula. After the plastic sheets have been prepared, the starch molecules are leached out of the membranes, thereby leaving tiny "pores" in the membranes. The diameters of the "pores" can be varied from 3 to 300 micra by using inert substances having different molecular sizes. The per cent porosity of the membranes can be varied by altering the per cent of inert material added. These studies have shown the permeability of these new membranes to be more dependent on the pore size and per cent porosity than on the type of plastic used.

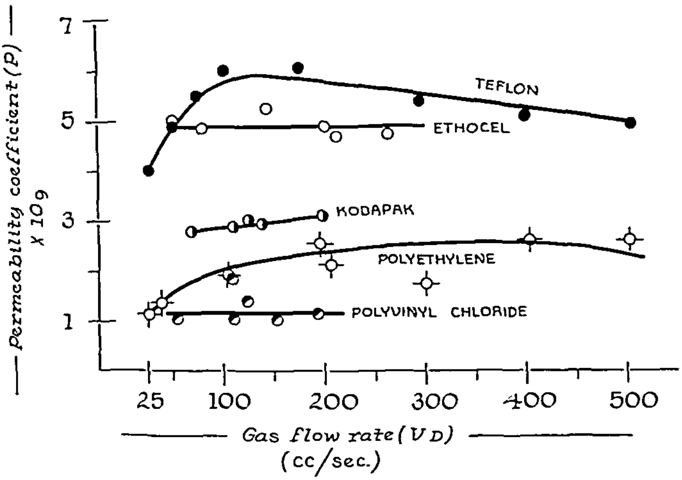

Fig. 4.—Permeability coefficients as a function of gas flow rate as measured with this apparatus.

Table I lists the carbon monoxide permeability coefficients determined with this apparatus and the coefficients for carbon dioxide obtained from the literature. Since the ratio of the permeability coefficients of two gases is relatively constant for almost all membranes, comparison of the ratios of the carbon monoxide permeability coefficients to those of carbon dioxide and oxygen provides a measure of the reliability of the data.

The permeability data obtained with this simple apparatus and technique warranted the further development of the experimental macroporous membranes and led to its production in larger sizes.

Partial perfusions of dogs with a small prototype oxygenator, using Teflon, Silastic, and N. P. Pormax membranes, were performed. The partial pressure

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*Supplied by Dr. Howard J. Strauss, ESB—Reeves Co., Glenside, Pa.

TABLE I*

MEMBRANE	P_{CO}	P_{O_2}	P_{CO_2}	$\frac{P_{CO_2}}{P_{O_2}}$	$\frac{P_{CO}}{P_{O_2}}$	$\frac{P_{CO}}{P_{CO_2}}$
Polyvinyl chloride	1.2	—	12[16]	—	—	0.10
Polyethylene	2.5	4.1[16]	18[16]	4.4	0.6	0.14
Cellulose acetate butyrate (Kodapak II)	3.2	—	35[16]	—	—	0.09
Ethylcellulose (Ethocel)	5.4	10[16]	43[10]	4.3	0.54	0.13
Tetrafluoroethylene (Teflon)	5.8	—	—	—	—	—
Natural rubber	18	32.7[16]	163[16]	5.0	0.55	0.11
Silicone rubber (Silastic S-2000)	375	650[10]	3,400[10]	5.2	0.58	0.11
N. P. Pormax	13,000-16,000	—	—	—	—	—
E. P. Pormax	15,000-25,000	—	—	—	—	—
Micro-Pormax	22,000-40,000	—	—	—	—	—

*Permeability coefficients at 30° C. P. = c.c.-mm./sec.-cm.^{2}-cm. Hg × 10^9 corrected to STP.

of the oxygen in the blood leaving and entering the animal was continuously monitored with oxygen electrodes.[21] Thus the effects of varying blood and oxygen flow rates and pressures could be noted immediately.

The average oxygen uptake for 0.00045 in. thick Teflon was 15 c.c. per minute per square meter. This compared with the average uptake of approximately 12 c.c. per minute per square meter reported by Pierce.[19] Silastic, 0.0068 in. thick, provided an uptake of 24 c.c. of oxygen per minute per square meter. Using N. P. Pormax with average pores of 8 to 12 micra, the oxygen uptake initially was over 35 c.c. of oxygen per minute per square meter when the oxygen pressure was one atmosphere. Because of the large pore size, however, blood rapidly leaked through the membrane into the oxygen chambers. This was only partially corrected by eliminating all wetting agents from the formulation but blood continued to "ooze" through when the pressure of the blood was greater than 30 mm. Hg. Inherent resistance to flow of blood in the oxygenator demanded a pressure greater than this. By increasing the oxygen pressure, the ooze could be further decreased and the oxygenation greatly increased. However, at a critical pressure, fine bubbles would appear in the blood. Presently new membranes are being prepared with 'smaller pores for evaluation.

SUMMARY

The advantage of using the concept of a permeability coefficient for indicating the relative permeability of different membranes to gases is described along with a simple apparatus and technique for determining the coefficients. This method permits the rapid screening of new membranes for possible use in a membrane oxygenator without testing different thicknesses of the same membrane or using an oxygenator with all the problems and expense it entails.

The permeability coefficients of several standard membranes and new plastic membranes containing "pores" which can be varied in diameter from 3 to 300 micra are listed and the membranes described.

Preliminary tests in a prototype oxygenator indicate these new membranes have superior oxygenating capacities but need development of membranes with smaller pore sizes.

REFERENCES

1. Van Amerongen, C. J.: Influence of Structure of Elastomers on Their Permeability to Gases, J. Polymer Sc. 5: 307, 1950.
2. Barrer, R. M.: Diffusion In and Through Solids, London, 1941, Cambridge University Press, p. 60.
3. Barrer, R. M.: Diffusion In and Through Solids, London, 1941, Cambridge University Press, p. 403.
4. Barrer, R. M., and Skirrow, G.: Transport and Equilibrium Phenomena in Gas-Elastomer Systems. I. Kinetic Phenomena, J. Polymer Sc. 3: 549, 1948.
5. Benvenuto, R., and Lewis, F. J.: Influence of Some Physical Factors Upon Oxygenation With a Plastic Membrane Oxygenator, Surgery 46: 1099, 1959.
6. Brubaker, D. W., and Kammermeyer, K.: Flow of Gases Through Plastic Membranes, Indust. Eng. Chem. 45: 1148, 1953.
7. Clowes, G. H. A., Neville, W. E., Sabga, G., and Shibota, Y.: The Relationship of Oxygen Consumption, Perfusion Rate, and Temperature to the Acidosis Associated With Cardiopulmonary Circulatory Bypass, Surgery 44: 220, 1958.
8. Clowes, G. H. A., Hopkins, A. L., and Neville, W. E.: An Artificial Lung Dependent Upon Diffusion of Oxygen and Carbon Dioxide Through Plastic Membranes, J. THORACIC SURG. 32: 630, 1956.
9. Doty, P. M., Aiden, W. H., and Mark, H.: Water Vapor Permeability of Organic Films, Indust. Eng. Chem., Anal. Ed. 16: 686, 1944.
10. Dow Corning Corp., Midland, Mich., Personal communication, 1959.
11. Hancher, C. W., and Kammermeyer, K.: Semiautomatic Gas Separation Equipment, Anal. Chem. 27: 83, 1955.
12. Jost, W.: Diffusion in Solids, Liquids, Gases, New York, 1952, Academic Press, N. Y., p. 297.
13. Jost, W.: Diffusion in Solids, Liquids, Gases, New York, 1952, Academic Press, N. Y., p. 285.
14. Kammermeyer, K.: Silicone Rubber as a Selective Barrier, I. E. C. 49: 1685, 1957.
15. Linderholm, H., Danielson, G. K., and Blakemore, W. S.: (To be published.)
16. Osburn, J. O., and Kammermeyer, K.: Separation of Gases by Plastic Membranes, New Diffusion Cell Design, Indust. Eng. Chem. 46: 739, 1954.
17. Othmer, D. F., and Frohlich, G. J.: Correlating Permeability Constants of Gases Through Plastic Membranes, Indust. Eng. Chem. 47: 1034, 1955.
18. Park, W. R. R.: Semimicro Gas Permeability Apparatus for Sheet Material, Anal. Chem. 29: 1897, 1957.
19. Pierce, E. C.: Diffusion of Oxygen and Carbon Dioxide Through Teflon Membranes, A. M. A. Arch. Surg. 77: 938, 1958.
20. Rosen, B., and Singleton, J. H.: Automatic Recording, Gas Polymer Film Permeater, J. Polymer Sc. 25: 225, 1957.
21. Schuder, J. C., McMichael, H., McCaughan, J. S., and Kirby, C. K.: Simplified Monitor and Control Devices for Artificial Heart-Lung Machines, Tr. Am. Soc. Artificial Int. Organs, 1958.
22. Shuman, A. C.: Apparatus for Measuring the Gas Permeability of Film Materials of Low Permeability, Indust. Eng. Chem., Anal. Ed. 16: 58, 1944.
23. Simril, V. L., and Hershberger, A.: Permeability of Polymer Films to Organic Vapors, Modern Plastics 27: 95, 1950.
24. Stannett, V., and Szwarc, M.: The Permeability of Polymer Films to Gases—A Simple Relationship, J. Polymer Sc. 16: 89, 1955.
25. Waack, R., Alex, N. H., Frisch, H. L., Stannett, V., and Szwarc, M.: Permeability of Polymer Films to Gases and Vapors, Indust. Eng. Chem. 47: 2524, 1955.

(For Discussion, see page 631)

TEMPERATURE COMPENSATED, SELF-CALIBRATED OXYGEN MONITORING DEVICE*

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Winston-Salem, N. C.

THE OXYGEN CONTENT of blood during procedures involving extracorporeal circulation has presented many new problems and challenges in medical instrumentation. One of the problems is the continuous monitoring of oxygen tension (in both venous and arterial blood) during extracorporeal circulation. One method of oxygen determination is polarography. The polarographic method of chemical analysis, invented by Jaroslav Heyrovsky,[1] is based on the unique characteristics of the current-voltage curves obtained when solutions of electro-oxidizable or electro-reducible substances are electrolyzed in a cell in which one electrode consists of mercury falling dropwise from a capillary glass tube. From such current-voltage curves it is possible not only to identify but also simultaneously determine the concentration of several or all the reducible or oxidizable substances present, i.e., simultaneously obtain a qualitative and quantitative analysis of a solution. One branch of polarography involves the use of the amperometric method. This method is used to indicate concentration measurements based on the measurement of electrolysis current at a constant potential of the indicator electrode. With this method the electrolysis current is directly proportional to the concentration of the elements being measured. For the determination of oxygen concentration, a constant potential of 0.6 volts is maintained across the electrode. The electrode consists of a platinum cathode and a silver-silver chloride anode immersed in electrolyte. The electrolyte is a saturated solution of potassium chloride. The use of this method was limited to in vitro sampling until the adaptation by Clarke and associates[2] of a gas permeable membrane to the electrode. As the result, the continuous determination of blood oxygen tension in vivo became a reality. However, because of concentration-temperature relationships (Fig. 1) it was necessary to perform determinations in a solution maintained at a constant temperature to avoid thermal

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Developed with the assistance of James M. Davis, B.S., Western Electric Co., Inc.

Read at the Fortieth Annual Meeting of The American Association for Thoracic Surgery at Miami Beach, Fla., May 11-13, 1960.

*Available from International Medical Instrument Co., Wakefield, Mass.

distortion. This paper describes an instrument which permits the continuous monitoring of oxygen tension by the polarographic (amperometric) method with automatic compensation for the temperature characteristics of the oxygen electrode. In addition, a method for introducing the polarographic electrode into the blood under sterile conditions is described.

PHYSICAL DESCRIPTION

The monitoring system is divided into three parts, (1) the oxygen electrode, (2) the cuvette for the introduction of the electrode and temperature detection of blood, and (3) electronic circuitry and read-out which allows both direct read-out and recorder output. During the original development of this instrument, the Clarke[2] electrode was used. This electrode was used during the original clinical perfusions also. We are, however, developing an experimental oxygen electrode which is an integral part of the monitoring cuvette. The cuvette* is a plastic (Teflon) cube. A stainless steel tube is introduced through the Teflon cube. Perpendicular to the stainless steel tube is a chamber, at one end of which is an opening tangent to the stainless steel tube (Fig. 2). The electrode is inserted into the chamber. The surface of the electrode membrane produces a tangent to the contour of the stainless tube. Also perpendicular to the stainless steel tube and parallel with the electrode chamber is a hole into which is inserted a bead-type thermistor to make physical contact with the stainless steel tube. For clinical applications the cuvette, thermistor, electrode membrane, "O" ring, and electrolyte are autoclaved. The electrode is soaked in a solution of detergicide. The electrode is then assembled and introduced into the cuvette under sterile conditions. The cuvette is then placed in series with the arterial and/or venous line (Fig. 3). The description and evaluation of an autoclavable electrode will be described in a subsequent paper.

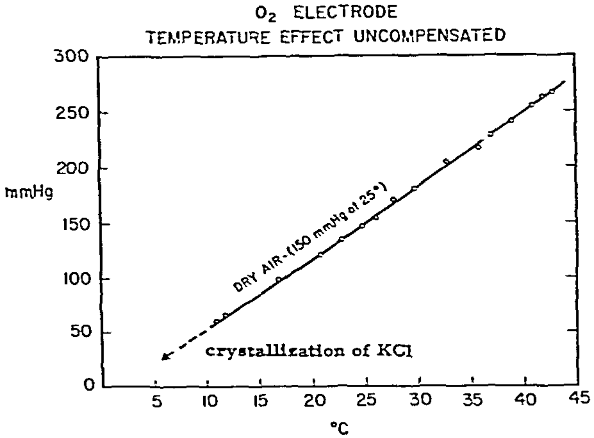

Fig. 1.—Graph showing oxygen tension versus temperature.

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*Designed by Leon L. Middleman, Winston-Salem, N. C.

The electronic read-out portions consist of an entirely portable, battery operated, and transistorized unit (Fig. 4). The amplifier portion is a transistorized differential DC amplifier. The direct read-out portion consists of a 5-inch meter (Fig. 5) which is calibrated in units of millimeters of mercury on four scales which are as follows: 0-75, 0-150, 0-300, 0-750. The recorder

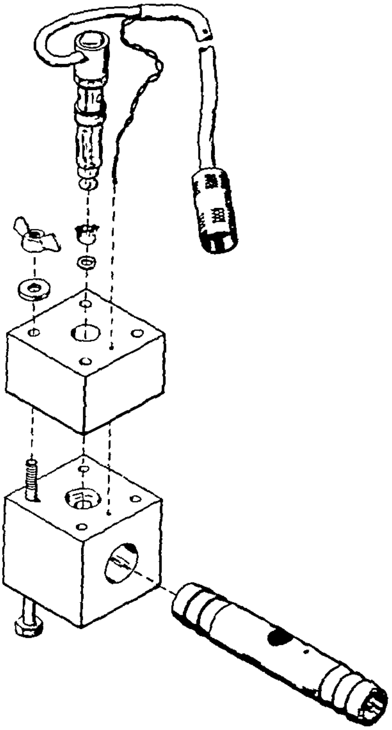

Fig. 2.—Cuvette isometric.

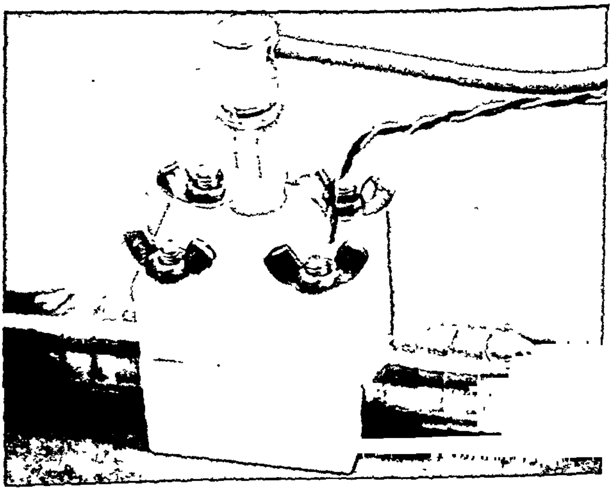

Fig. 3.—The assembled cuvette.

output portion consists of a single transistor amplifier capable of delivering sufficient output to drive most conventional recorders.

The depolarizing oxygen potential of 0.6 volts is supplied to the electrode from a battery circuit and the potential maintained within the depolarizing potential of oxygen by means of zener diode voltage regulator

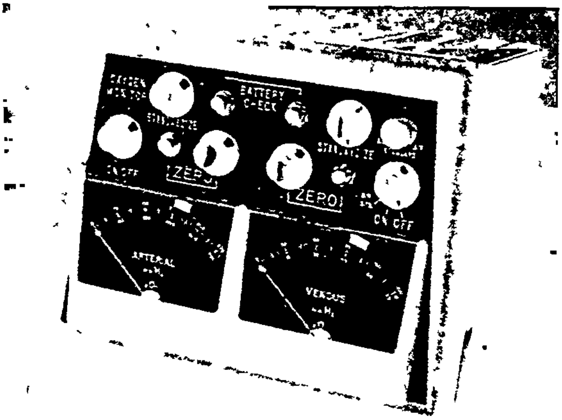

Fig. 4 —Photograph of unit.

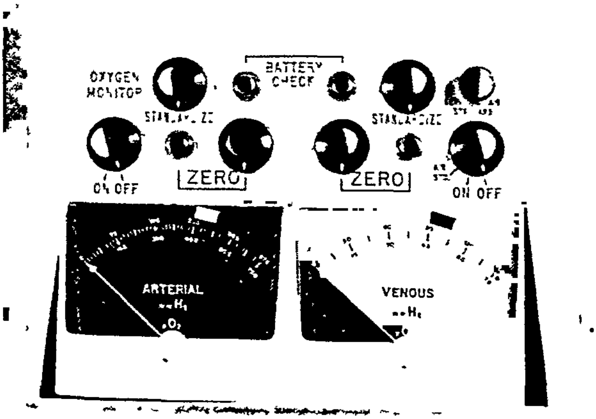

Fig 5 —Photograph of meter face

Temperature compensation is achieved by the inclusion of a thermistor (Fig. 6), which is physically located in the cuvette. The requirements for temperature compensation via thermistor are that the ratio of resistance of the thermistor be as great as or greater than the ratio of the change of current output of the electrode due to temperature. The differential DC amplifier configuration assures stable operation even in the presence of atmospheric changes. The unit is standardized by exposing the electrode to room air. Under these conditions the standardized control is moved until the partial pressure of oxygen present in room air is indicated on whichever of the four scales is desired. This method of standardization allows stable operation of the electronic circuitry regardless of the full scale range selected. The use of a transistorized circuit has resulted in several advantages: (1) the adaptability of a power supply which allows the unit to become completely portable and eliminates the necessity of power connection, (2) the physical size of the transistor circuitry allows the unit to be compact and easily portable, (3) the exceptionally low power requirements of transistor circuitry permits extended battery life. The device will operate for approximately 1,000 hours without battery replacement. In addition, the operation of a push-button type switch allows the periodic checking of the batteries. Although this system was designed and developed for use during total body perfusion and this paper will be confined to that application, several other applications of the device have been noted and are being currently appraised. They are: (1) monitoring of O_2 during regional perfusion for cancer chemotherapy, (2) the location of shunts during cardiac catheterization, and (3) as part of an experimental instrumentation system for the determination of O_2 consumption of various organs in vivo. For purposes of total body perfusion, a double unit is used; one continuously indicating the oxygen tension of arterial blood and the second unit continuously indicating the oxygen tension of venous blood. The electrodes are standardized in room air under sterile conditions prior to their insertion into the cuvette. They are checked in blood during a recirculation period. During this time both the venous and arterial oxygen tension will be identical. This reading during recirculation allows the adequate pre-perfusion oxygenation of the priming blood. During the initial use of this instrument during perfusion, it was noted that the oxygen tension of donor blood remained relatively low for a long period of time even during recirculation. This period of low oxygen tension during recirculation and oxygenation is a result of oxygen uptake by the hemoglobin with a minimal

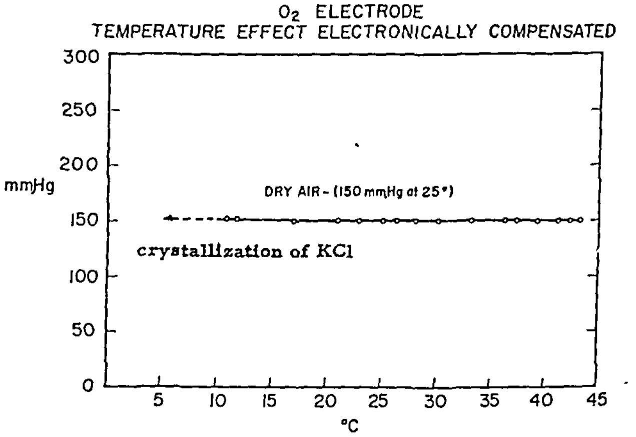

Fig. 6.—Graph showing oxygen tension versus temperature with electronic compensation.

elevation of the partial pressure of oxygen. By periodic sampling or the use of a continuous pH monitor, it was demonstrated that during the period of recirculation the pH of the priming blood increased. As a result of these observations the degree of oxygenation of priming blood and the control of pH was maintained and brought to normal point prior to the time of going on bypass. Close contact is maintained with the surgeon upon going on full bypass. The venous oxygen monitor is watched for the first bolus of patient blood passing through the cuvette. This bolus of blood will give an indication of the patient's venous oxygen tension. During normothermia this level is readily maintained; however, during hypothermia and severe hypothermia, a decrease in venous oxygen tension has been noted. This decrease in plasma oxygen tension is reasonable when one considers the increased combining power of hemoglobin at a lowered temperature.

The oxygen monitor has been used during clinical perfusions and laboratory experiments. It has been found to be a valuable instrument which allows continuous monitoring of this vital parameter.

SUMMARY

This paper describes an instrument which permits the continuous monitoring of oxygen tension in vivo during normothermia and severe hypothermia. A method for introducing the detecting device into blood under sterile conditions and the electronic circuitry are described.

REFERENCES

1. Jaroslav Heyrovsky: Chem. Listy 16: 256, 1922.
2. Clarke, L. C., Wold, R., Granger, R., and Taylor, Z.: J. Appl. Physiol. 6: 189, 1953.

(For Discussion, see page 631)

PULMONARY ARTERIAL HYPEROXIA PRODUCING INCREASED PULMONARY VASCULAR RESISTANCE

Peter V. Moulder, M.D., Joseph R. Lancaster, M.D. (by invitation), Robert W. Harrison, M.D. (by invitation), Stephen L. Michel, B.S. (by invitation), Mark Snyder, M.D. (by invitation), and Richard G. Thompson, M.D. (by invitation), Chicago, Ill.

THE RELATIONSHIP of oxygen and lack of oxygen to the pulmonary circulation has been intensively studied in the laboratory and the relationship has been further used in cardiac catheterization studies, as well as being applied to clinical medicine. In 1946 von Euler and Liljestrand[1] first demonstrated the effect of hypoxia on the pulmonary circulation with the induction of pulmonary hypertension. This was further demonstrated in normal human beings and in patients with disease of the pulmonary vascular circulation in 1947 by Motley and Cournand,[2] and by many others[3, 4, 5] in subsequent years. There has not been a clear-cut refutation of this effect of hypoxia in human studies. Helen Duke[6] has demonstrated this same hypoxic effect in elaborate perfusion and cross-circulation experiments in cats. Others have found this reaction in cats, rabbits, and dogs.[7-10] Although there are still repeated observations on hypoxia increasing pulmonary vascular resistance, there have appeared recently a few studies[11-14] which show no such effect. The most critical and neatest set of observations were those of Nahas and co-workers[11] in unanesthetized dogs trained for study in whom the effect of hypoxia in chamber breathing revealed no increased pulmonary vascular resistance. This study emphasized the fact that the Fick method of measuring cardiac output was unreliable in these unsteady states of hypoxia and that the dye curve method of Stewart and Hamilton was the most useful system. Nahas demonstrated that, although the pulmonary pressure became elevated, it was merely a reflection of an increased cardiac output and that there was little change in the vascular resistance in the lungs.

There has been little or no experimental work on the effect of oxygen at the pulmonary arterial level. There have been sporadic studies related to inspired oxygen concentration changes and to systemic-pulmonary shunts. Breathing 100 per cent oxygen, as well as the injection of certain drugs, such as acetylcholine and aminophylline, has been used to demonstrate lability of the pulmonary vascular bed in the patient with pulmonary hypertension. Ferguson and Varco[15, 16] and Muller and Dammann[17] have studied the effects of systemic

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to pulmonary arterial shunts on the pulmonary circulation, and, in general, the attempt to produce pulmonary hypertension without the separation of a lobe from the pulmonary circulation has been disappointing. Studies of large left-to-right shunts from the systemic circulation to the right atrium in this laboratory[18] have shown minimum effect on the pulmonary vascular resistance. In the studies in dogs by Boake, Daley, and McMillan,[19] in 1959, studying the effect of a partial reoxygenated circulation (extracorporeally produced) in reversing hypoxic-induced pulmonary hypertension, a slight increase in pulmonary arterial pressure was noted when the extracorporeal circuit was added to the normal circulation.

These experiments were planned to approach complete control of the blood and atmospheric oxygen concentrations contacting the pulmonary vascular bed so that the inter-relationship of these two could be studied. The findings of a tremendous increase in pulmonary vascular resistance with the introduction of oxygenated blood to the pulmonary circulation has overshadowed the study of the relationships of inspired gas to blood-gas concentration.

METHOD

Healthy mongrel dogs, weighing from 18 to 22 kilograms, received 2 mg. per kilogram of morphine sulfate subcutaneously followed by Thiobarbital (2.5 per cent) administered intravenously until light anesthesia was obtained. Open tracheostomy with a large, securely-fitting metal cannula allowed complete control of the gas mixtures used for ventilation. The gas was delivered from tanks containing various percentages of nitrogen and oxygen and an intervening Rattenborg[20] valve, which allowed for dissipation of the expired gas and continuous replacement of the inspired gas with the planned concentration from the gas cylinder. With the thorax open, ventilation was performed manually at the rate of 18 per minute with sufficient volume to bring the lungs to the chest wall. Right thoracotomy through the fifth intercostal space was performed and cannulations with large bore catheters were made as follows: through the azygos vein—right atrium and right ventricle; through a small branch of the pulmonary vein—left atrium; and through a branch of the pulmonary artery—central pulmonary artery, and a separate catheter placed with this was used for withdrawing pulmonary arterial blood samples for analyses. Statham P23G, P23D, or P23DC pressure transducers were used and all records were taken on a six-channel Grass polygraph with Lead II electrocardiogram.

Indocyanine green dye dilution curves were performed for estimation of the cardiac output. These were recorded on a Texas direct writing rectilinear galvanometer at a paper speed of 12 in. per minute. The dye was injected rapidly into the right ventricle and blood was withdrawn from the thoracic aorta at a rate of 80 ml. per minute. Gilford withdrawal syringe and densitometer were used. Sodium heparin was given intravenously at a dose of 2 mg. per kilogram just before instituting extracorporeal circulation. Cannulations were performed as follows: the superior vena cava was drained via a large catheter passed through the external jugular vein to a point above the azygos vein in the superior vena cava with total occlusion by tape tie obtained when bypass was instituted; a large bore catheter was placed in the inferior vena cava after it was ligated and opened to assure total bypass; venous blood was drained by gravity to a well; shunted blood was returned from an overflow well system at a constant level above the right atrium via a large catheter in the right atrial appendage, and the overflow from this double funnel system drained to a well parallel with the caval drainage one. These were then pumped by means of a Sigmamotor TM4 pump through a Brown-Harrison heat exchanger and Abbott stainless steel mesh filter to the constant level reservoir. For oxygenation of the venous blood, the blood from the two wells was shunted through a double set of bubble oxygenators, Pulmo-Paks,* and thence returned to the venous overflow reservoir for subsequent return to the right atrium. Fig. 1 demonstrates the relationship of these various catheters in the chest and in Fig. 2 the extracorporeal setup for returning venous blood or oxygenated blood. The pump speed is fixed to produce constant overflow at all times and the system primed with fresh, compatible, heparinized dog blood. Temperature control was maintained with the use of the heat exchanger in the circuit and temperatures were monitored with a Yellow Springs telethermometer by thermistor probes in the constant level reservoir, rectum, and in deep neck muscle.

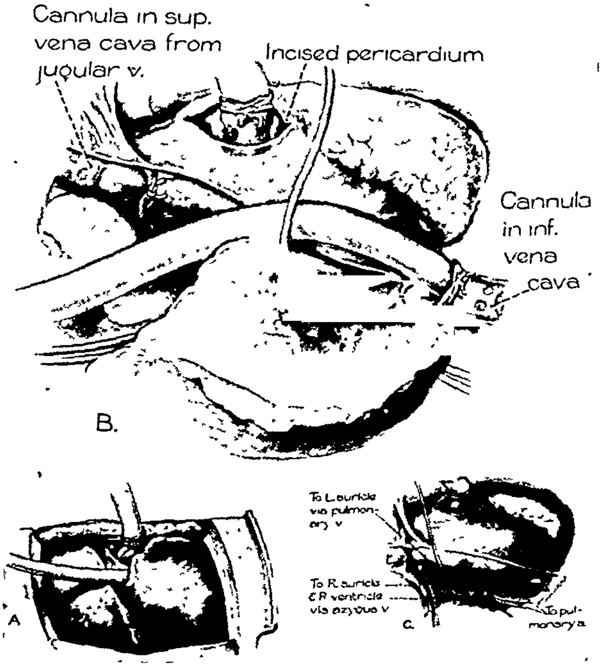
Cannula in sup. vena cava from jugular v.
Incised pericardium
Cannula in inf. vena cava
B.
A
To L auricle via pulmonary v
To R auricle & R ventricle via azygous v
To pulmonary a.
C.

Fig. 1.—Position of blood catheters and measuring cannulae. *A*, During study period catheter positions are such as not to interfere with motion of lung. *B*, The caval cannulae positioned to ensure complete venous drainage. *C*, The sites of the various catheters for pressure measurements and other studies.

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*Pulmo-Pak bubble oxygenators were generously supplied by Dr. Rodney Gwinn of Abbott Laboratories.

After cannulations were completed except for the one in the inferior vena cava, the control readings were obtained. After cannulation of the inferior vena cava and the initiation of simple bypass, the level of the constant reservoir was adjusted to reproduce nearly right atrial and systemic pressure without elevation of right ventricular diastolic pressure. This was surprisingly constant at a level of 20 cm. above the table and about 10 cm. above the superior vena cava-right atrial junction. Electrolyte and acid-base chemical analyses and microhematocrit determinations were performed on thoracic aortic blood by standard methods[21]; blood oxygen saturation and CO_2 content were determined by Van Slyke procedures[22] on thoracic aortic blood, pulmonary arterial and venous well blood to represent mixed venous sample when bypass oxygenation was instituted.

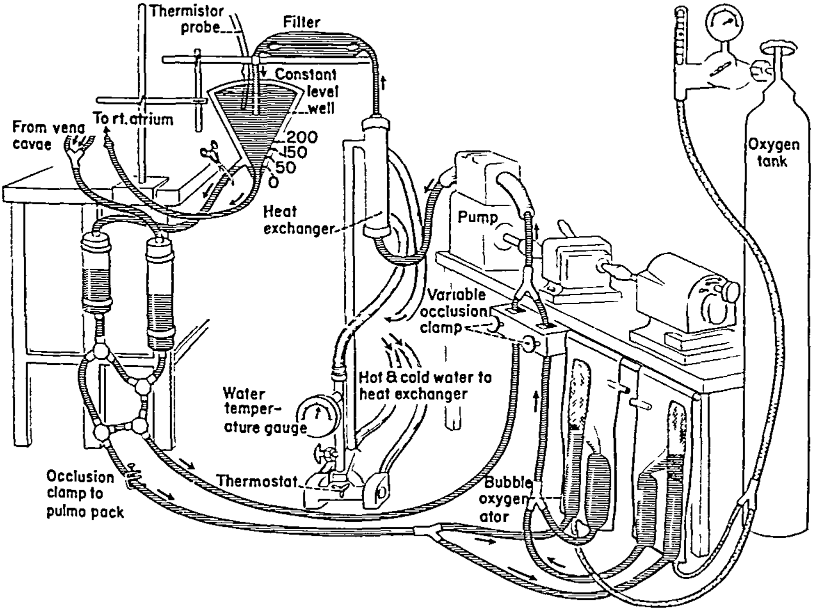

Fig. 2.—Diagrammatic presentation of the various elements in the extracorporeal circuit which allowed return of venous blood or oxygenated blood from a constant level overflow reservoir with Brown-Harrison heat exchanger for temperature control.

RESULTS

Eleven useful experimental preparations were obtained (if the procedure had been excessively traumatic or pressure pulse curves were not adequate for study, or if there had been a period of failure or difficulty with the heart, the study was not continued). Ten of these animals were prepared as just described with an irreversible bypass in which certainty of total venous circulatory bypass was desired (exclusive of coronary venous blood). However, one animal was prepared for reversible bypass in which the inferior caval cannulation was performed through the right atrial wall.

Of the 10 dogs with irreversible bypass, there were slight variations in pattern. First, the initial searching studies were primarily aimed toward studying the relations of expired blood gas and, as the hyperoxygenation effect was noted, the pattern of study was modified accordingly. Measurement of pulmonary wedge pressure, in order to see an effect on the pulmonary veins between pulmonary wedge and left atrium, was attempted, but good curves were obtained so infrequently that these data are useless. Use of overflow blood as an indicator of cardiac output proved to be a surprisingly misleading method: the pump was set at a fixed output, the amount of blood from a timed collection in the overflow system subtracted from the predetermined output of the pump, and flow from the reservoir to right atrium was calculated; however, this proved to be unrelated to dye dilution curve studies. Second, some of these animals during the run actually died from the induced pulmonary hypertension. This is graphically demonstrated in Fig. 3, in which an animal with abnormally high initial resistance of 871 dyne sec. cm.$^{-5}$, associated with a pulmonary arterial oxygen saturation of 35 per cent, shows an increasing resistance to 1,137 on bypass and, with oxygenation, a striking increase in pulmonary artery pressure demonstrated on the slow speed record of pressures. After a short time on the bypass with oxygenator, there is a decrease in cardiac output with a tremendous increase in vascular resistance to 4,752 dyne sec. cm.$^{-5}$ Shortly thereafter, the

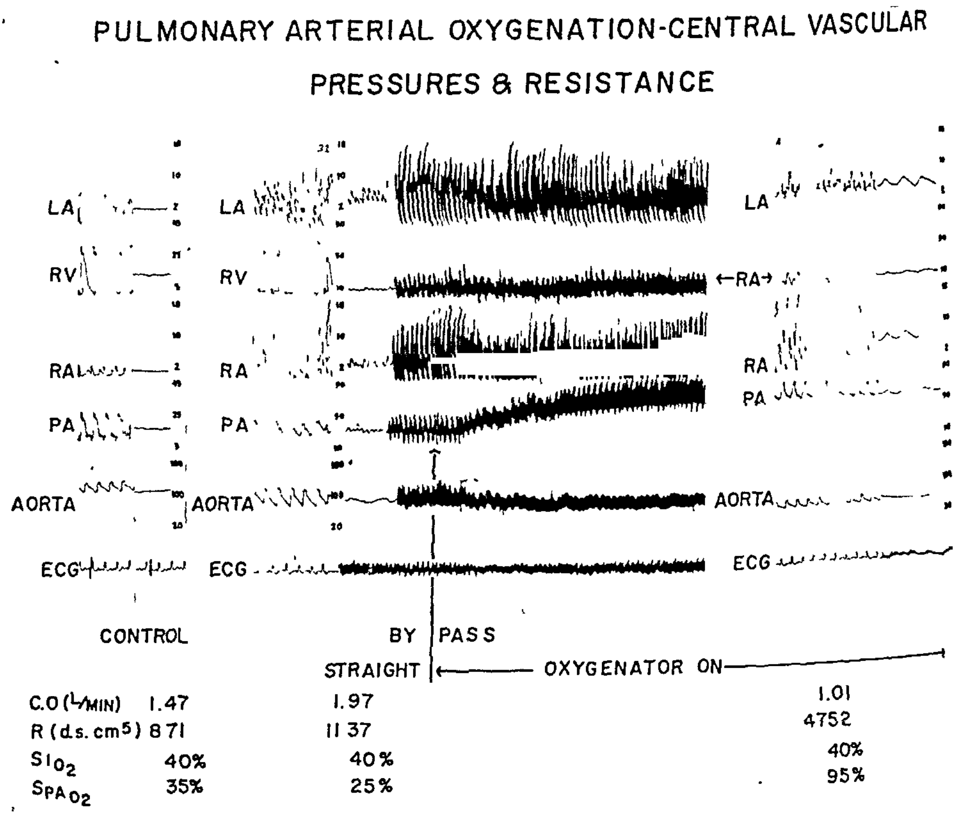

Fig. 3.—Reproduction of segments of the original pressure pulse traces with oxygen values and calculated cardiac output and pulmonary vascular resistances obtained on a dog developing a lethal increase in pulmonary vascular resistance under the stimulus of oxygenated blood. The rise in pulmonary arterial pressure is seen in the central panel with recording at slow speed.

right heart failed and death ensued. Third, the use of 8 per cent oxygen in the inspired gas concentration produced a pattern of such rapid deterioration that an adequate study could not be performed; therefore, in subsequent experiments, stabilization at higher oxygen concentration was performed first.

Three experiments were performed in almost precisely the same pattern. In these three, there were nine separate stages of study: (1) control run without bypass with the animal breathing 40 per cent oxygen; (2) simple bypass, breathing 40 per cent oxygen; (3) bypass with oxygenator, breathing 40 per cent oxygen; (4) bypass with oxygenator, breathing 8 per cent oxygen; (5) bypass with oxygenator, breathing 100 per cent nitrogen, no oxygen; (6) bypass with oxygenator, breathing 20 per cent oxygen; (7) simple bypass, breathing 20 per cent oxygen; (8) bypass with oxygenator, breathing 8 per cent oxygen; and (9) simple bypass, breathing 8 per cent oxygen. Three readings were made in the ninth stage before termination of the experiment and, because of the low oxygenation, usually pre-terminus in the animal. Table I lists these data obtained on the 3 animals carried through this experiment.

One experiment was performed as described with ability to come off the oxygenator and bypass completely, and this served to corroborate the findings with the irreversible bypass.

In general, on the circulatory bypass, with or without oxygen, there was some increase in pulmonary arterial pressure and pulmonary vascular resistance. This is demonstrated in Fig. 4, in which the various stages, as just described, on the 3 strictly comparative animals are presented, with variations from the control measurement base line averaged and graphed in percentage deviations. At all times on the bypass, the 3 animals showed increased pulmonary artery minus left atrial mean pressure and increases in total pulmonary resistance with minor variations in cardiac output. However, the presence of the oxygenating shunt was associated with the most marked increases in vascular resistance. There is a suggestion in the pattern seen in stages 3, 4, and 5, in which the respiratory gas oxygen concentration was decreased, that there might be an additive effect of the inspired low gas oxygen concentration. However, this was not necessarily true in other experiments and, since there is variation in the $S_{PA_{O_2}}$, this would be attempting to extract too much from the data with reference to this one variable.

The experimental setup was associated with a remarkably stable pulse, electrocardiogram, and central aortic pressure, which lends validity to these data. Fig. 5 presents segments of the pressure curves and electrocardiogram from one such experiment (right ventricular pressure was on another polygraph at this time when a pulmonary wedge pressure was being sought). The uselessness of the wedge curve throughout the experiment is apparent. There is an increase in phasic and mean pulmonary artery pressures when bypass is instituted, and these further increase with the oxygenator. There is a reversion with the oxygenator off, although they remain higher than those prior to institution of bypass. The importance of the recording of left atrial phasic and mean pressures can be seen in the third and fourth panels when the atrial pressure has also risen with the pulmonary artery pressure and accuracy can be obtained

DOG NO.	CONDITION	TEMPERATURE (° C.)			BLOOD						CHEMIS SERU (MEq.	
					MIXED VENOUS		PULMONARY ARTERY		AORTA			
		RECTAL	MUSCLE	BLOOD	O_2 SAT. (%)	CO_2 (VOL. %)	O_2 SAT. (%)	CO_2 (VOL. %)	O_2 SAT. (%)	CO_2 (VOL. %)	Na	K
1	Control Run Pre-Bypass Breathing: 60% N_2—40% O_2	37.0	37.0	–	–	–	40.88	40.88	95.62	27.63	–	–
2		37.0	37.0	–	–	–	32.4	–	95.9	–	–	–
3		–	35.0	–	–	–	60.83	31.25	85.11	31.02	–	–
1	Straight Bypass Breathing: 60% N_2—40% O_2	36.2	36.5	38.0	–	–	43.84	33.18	87.49	28.09	139	4.5
2		37.2	37.5	38.0	–	–	49.33	32.73	100.43	23.18	145	3.3
3		–	36.2	38.0	–	–	53.94	28.90	86.15	22.63	144	4.8
1	Bypass Oxygenator On Breathing: 60% N_2—40% O_2	36.6	36.7	37.8	43.31	32.53	96.01	20.23	95.57	20.18	–	–
2		37.0	37.8	38.5	52.23	29.44	94.76	22.11	98.79	17.96	–	–
3		–	36.5	37.2	60.13	24.16	80.25	22.56	100.79	15.57	–	–
1	Bypass Oxygenator On Breathing: 92% N_2—8% O_2	36.6	36.5	37.5	44.72	27.86	91.33	18.94	91.09	18.15	–	–
2		37.0	38.0	38.4	46.64	26.46	89.94	18.49	89.51	16.70	–	–
3		–	36.2	37.0	50.05	24.51	106.83	17.26	94.84	15.36	–	–
1	Bypass Oxygenator On Breathing: 100% N_2	36.5	36.4	37.7	46.13	26.95	101.22	20.72	89.93	17.54	–	–
2		37.3	38.2	38.0	30.87	23.48	97.40	19.27	67.89	14.08	–	–
3		–	37.0	37.0	41.45	22.09	98.23	16.25	91.68	15.45	–	–
1	Bypass Oxygenator On Breathing: 80% N_2—20% O_2	36.5	36.4	37.7	–	–	–	–	–	–	–	–
2		37.4	38.1	38.0	–	–	–	–	–	–	–	–
3		–	37.0	38.0	–	–	–	–	–	–	–	–
1	Bypass Oxygenator Off Breathing: 80% N_2—20% O_2	36.2	36.6	38.0	–	–	53.58	24.29	63.70	22.80	141	4.5
2		37.0	38.0	38.2	–	–	43.24	23.68	72.93	20.30	144	3.0
3		–	37.0	38.0	–	–	23.10	27.82	52.18	21.33	138	4.6
1	Bypass Oxygenator On Breathing: 92% N_2—8% O_2	–	–	–	–	–	–	–	–	–	–	–
2		37.0	38.0	37.5	–	–	–	–	–	–	–	–
3		–	–	–	–	–	–	–	–	–	–	–

(Continued on next pages.)

BLOOD					PRESSURES (MM. HG.)						CARDIAC OUTPUT (L./MIN.)	TOTAL PULM. RESISTANCE (DYNE SEC. CM.$^{-5}$)
MISTRIES SERUM MG. %)			CELL VOLUME (%)	PULSE	RIGHT ATRIUM	RIGHT VENTRICLE	PULMONARY ARTERY	LEFT ATRIUM	AORTA	MEAN PA-LA		
a	P	NPN										
	–	–	47	135	2/0 M = 1	30/0	30/8 M = 17	12/8 M = 10	120/90 M = 100	7	1.23	455
	–	–	52	170	6/0 M = 2	30/0	28/10 M = 13	4/0 M = 1	140/110 M = 120	12	2.18	440
	–	–	45	152	4/0 M = 2	22/0	21/5 M = 10	3/0 M = 2	90/60 M = 70	8	1.56	410
.5	5.5	–	–	125	2.5/–1 M = 1.5	30/0	30/19 M = 25	8/5 M = 7	140/105 M = 120	18	1.33	1083
.5	6.0	28	52	120	6/2 M = 4	30/0	30/15 M = 20	3/0 M = 1	160/110 M = 130	19	1.98	768
	–	33	45	147	4/0 M = 1.5	25/0	23/10 M = 13	3/0 M = 2	90/60 M = 70	11	1.74	506
	–	–	50	130	4.5/2.5 M = 3.5	40/2	40/30 M = 34	15/8 M = 11	150/100 M = 120	23	1.13	1628
	–	–	49	143	9/5 M = 8	38/2	38/20 M = 27	5/0 M = 3	160/110 M = 120	24	1.79	1073
	–	–	41	139	4/0 M = 2.2	26/0	26/15 M = 18	3/0 M = 2	100/75 M = 85	16	1.70	753
–	–	–	46	170	4/0 M = 3	40/1.5	40/27.5 M = 30	10/6 M = 9	140/95 M = 110	21	1.20	1400
–	–	–	49	182	11/7 M = 8	43/3	43/27 M = 35	3/0 M = 1	150/100 M = 110	34	1.98	1374
–	–	–	47	140	6/2 M = 4	32/0	35/25 M = 27	3/1 M = 2	100/80 M = 85	25	1.97	1015
–	–	–	44	170	4/0.5 M = 3.5	40/4	40/32.5 M = 35	11/7 M = 10	145/100 M = 110	25	1.05	1905
–	–	–	52	160	5/2 M = 4	37/0	35/20 M = 25	3/0 M = 1.5	115/80 M = 100	23.5	2.09	900
–	–	–	45	170	4/0 M = 2	35/0	35/27 M = 31	3/0.5 M = 2	85/65 M = 70	29	1.68	1381
–	–	–	–	170	3.5/0.5 M = 3.0	45/5	45/32.5 M = 35	10/4 M = 8.5	135/100 M = 110	26.5	0.93	2279
–	–	–	–	200	7/2 M = 5	N.G.	35/20 M = 25	3/0 M = 1	105/75 M = 90	24	1.88	1021
–	–	–	–	148	6/2 M = 4	36/0	42/26 M = 32	4.5/1 M = 2.5	95/60 M = 80	29.5	1.91	1236
9.5	6.6	–	44	170	8/5 M = 6.5	40/5	40/32.5 M = 35	12/8 M = 10	160/130 M = 140	25	1.34	1493
9.7	6.7	33	52	120	6/3 M = 5	37/0	37/20 M = 23	6/3 M = 4	120/90 M = 100	19	1.96	775
–	–	42	45	170	2.5/0 M = 1.5	30/0	30/20 M = 25	2/0 M = 1	80/55 M = 60	24	1.97	975
–	–	–	–	150	6/4 M = 5.5	40/2.5	40/32.5 M = 35	11/8 M=10.5	140/110 M = 115	24.5	1.15	1704
–	–	–	–	180	6/2 M = 4	N.G.	28/17 M = 22	2/0 M = 1	70/40 M = 60	21	1.76	955
–	–	–	–	177	4/0 M = 2	33/0	37/27 M = 31	2/0 M = 1	80/60 M = 70	30	1.52	1579

DOG NO.	CONDITION	TEMPERATURE (° C.)			BLOOD						CHEMIST SERU (MEq./	
					MIXED VENOUS		PULMONARY ARTERY		AORTA			
		REC-TAL	MUS-CLE	BLOOD	O_2 SAT. (%)	CO_2 (VOL. %)	O_2 SAT. (%)	CO_2 (VOL. %)	O_2 SAT. (%)	CO_2 (VOL. %)	Na	K
	Control Run											
1	Pre-Bypass	37.0	37.0	–	–	–	40.88	40.88	95.62	27.63	–	–
	Breathing:											
2	60% N_2—40% O_2	37.0	37.0	–	–	–	32.4	–	95.9	–	–	–
3		–	35.0	–	–	–	60.83	31.25	85.11	31.02	–	–
	Straight Bypass											
1	Breathing:	36.2	36.5	38.0	–	–	43.84	33.18	87.49	28.09	139	4.5
	60% N_2—40% O_2											
2		37.2	37.5	38.0	–	–	49.33	32.73	100.43	23.18	145	3.3
3		–	36.2	38.0	–	–	53.94	28.90	86.15	22.63	144	4.8
	Bypass Oxygenator											
1	On Breathing:	36.6	36.7	37.8	43.31	32.53	96.01	20.23	95.57	20.18	–	–
	60% N_2—40% O_2											
2		37.0	37.8	38.5	52.23	29.44	94.76	22.11	98.79	17.96	–	–
3		–	36.5	37.2	60.13	24.16	80.25	22.56	100.79	15.57	–	–
	Bypass Oxygenator											
1	On Breathing:	36.6	36.5	37.5	44.72	27.86	91.33	18.94	91.09	18.15	–	–
	92% N_2—8% O_2											
2		37.0	38.0	38.4	46.64	26.46	89.94	18.49	89.51	16.70	–	–
3		–	36.2	37.0	50.05	24.51	106.83	17.26	94.84	15.36	–	–
	Bypass Oxygenator											
1	On Breathing:	36.5	36.4	37.7	46.13	26.95	101.22	20.72	89.93	17.54	–	–
	100% N_2											
2		37.3	38.2	38.0	30.87	23.48	97.40	19.27	67.89	14.08	–	–
3		–	37.0	37.0	41.45	22.09	98.23	16.25	91.68	15.45	–	–
	Bypass Oxygenator											
1	On Breathing:	36.5	36.4	37.7	–	–	–	–	–	–	–	–
2	80% N_2—20% O_2	37.4	38.1	38.0	–	–	–	–	–	–	–	–
3		–	37.0	38.0	–	–	–	–	–	–	–	–
	Bypass Oxygenator											
1	Off Breathing:	36.2	36.6	38.0	–	–	53.58	24.29	63 70	22.80	141	4 5
2	80% N_2—20% O_3	37.0	38.0	38.2	–	–	43.24	23.68	72.93	20.30	144	3.0
3		–	37.0	38.0	–	–	23.10	27.82	52.18	21.33	138	4.6
	Bypass Oxygenator											
1	On Breathing:	–	–	–	–	–	–	–	–	–	–	–
2	92% N_2—8% O_2	37.0	38.0	37.5	–	–	–	–	–	–	–	–
3		–	–	–	–	–	–	–	–	–	–	–

(Continued on next pages)

DOG NO.	CONDITION	TEMPERATURE (° C.)			BLOOD							
					MIXED VENOUS		PULMONARY ARTERY		AORTA		CHEMIST SERU (MEQ./	
		REC-TAL	MUS-CLE	BLOOD	O_2 SAT. (%)	CO_2 (VOL. %)	O_2 SAT. (%)	CO_2 (VOL. %)	O_2 SAT. (%)	CO_2 (VOL. %)	Na	K
1	Bypass Oxygenator Off Breathing:	36.1	36.4	38.0	–	–	55.33	25.70	55.43	24.59	–	–
2	92% N_2—8% O_2	37.4	38.0	38.2	–	–	30.33	23.44	46.40	17.27	–	–
3		–	37.0	37.2	–	–	28.96	22.35	44.50	18.94	–	–
1	Bypass Oxygenator Off Breathing:	35.9	35.6	38.0	–	–	–	–	12.65	27.50	–	–
2	92% N_2—8% O_2	–	–	–	–	–	9.54	24.61	26.15	19.10	–	–
3		–	37.0	37.2	–	–	9.73	24.26	15.77	15.33	–	–
1	Bypass Oxygenator Off Breathing:	–	–	–	–	–	–	–	–	–	–	–
2	92% N_2—8% O_2	37.0	38.0	38.0	–	–	–	–	–	–	–	–

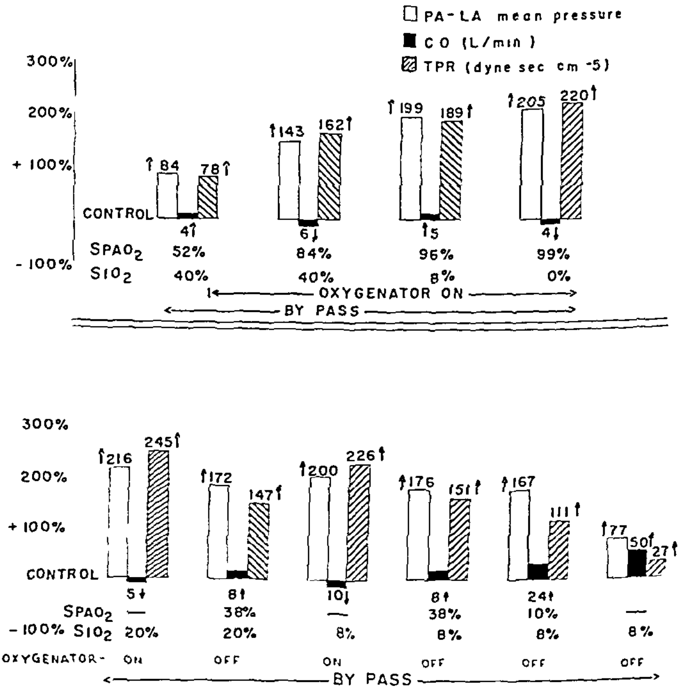

Fig. 4.—Comparison of the important circulatory findings in the nine stages of study on three experiments from the data in Table I. Each value is compared to its control level and the average percentage change for the three experiments is represented in the blocks for effective mean pulmonary artery pressure (PA-LA mean), cardiac output, and total pulmonary resistance.

'D

BLOOD					PRESSURES (MM. Hg.)						CARDIAC OUTPUT (L./MIN.)	TOTAL PULM. RESISTANCE (DYNE SEC. CM.$^{-5}$)
ISTRIES ERUM G %)			CELL VOLUME (%)	PULSE	RIGHT ATRIUM	RIGHT VENTRICLE	PULMONARY ARTERY	LEFT ATRIUM	AORTA	MEAN PA LA		
|	P	NPN										
	–	–	47	150	5/3 M = 4 0	40/1	40/32 5 M = 35	13/10 M = 12	165/135 M = 150	23	1.51	1219
	–	–	49	140	12/4 M = 6	30/0	30/20 M = 23	5/2 M = 3	138/100 M = 120	20	1.92	833
	–	–	48	170	4/0 M = 2	N G	37/25 M=27 5	2 5/0 M = 1	100/70 M = 80	26 5	1.74	1218
	–	–	–	50	14/5 M=N G.	40/4	40/25 M = 35	20/10 M = 14	200/130 M = 160	21	1 61	1043
	–	–	–	130	6/2 M = 5	N G.	30/15 M = 22	3/0 M = 1	120/90 M = 105	21	2.25	747
	–	–	–	178	4/0 M =2 5	N.G	40/25 M = 28	3/0 M = 2	100/55 M = 70	26	2.17	958
	–	–	–	80	12/2 M = 4	20/2	20/10 M = 15	5/2 M = 2 5	120/40 M = 60	12.5	2.35	426
	–	–	–	110	7/2 M = 5	N.G	33/15 M = 22	3/0 M = 1	100/65 M = 90	21	2 40	700

PULMONARY ARTERIAL OXYGENATION-CENTRAL VASCULAR PRESSURES & RESISTANCE

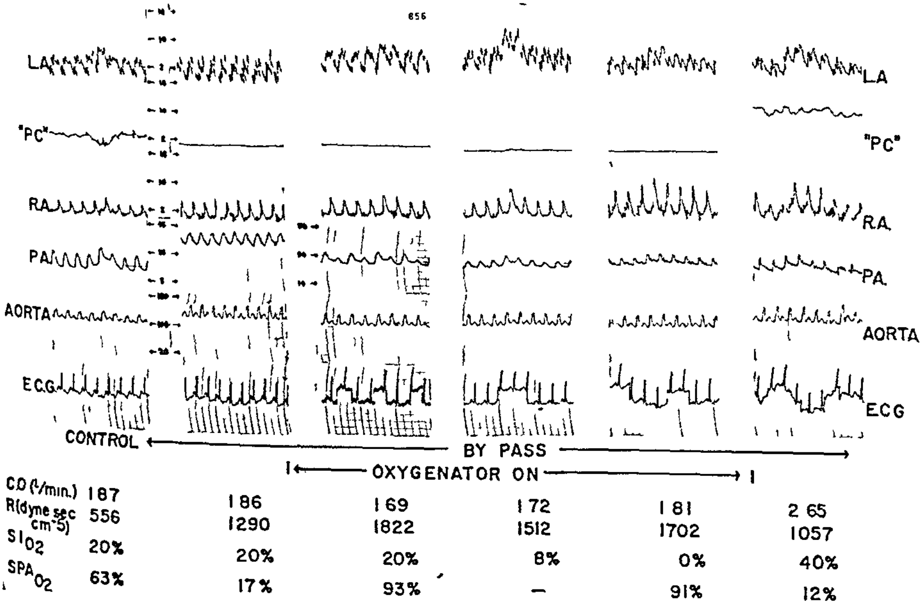

Fig 5 —Segments of original pressure pulse traces with the oxygen data and calculated cardiac output and total pulmonary resistance for one experiment demonstrating characteristic changes associated with bypass, and bypass with oxygenation and, under these circumstances, no added effect from decrease in inspiratory oxygen concentration (SI_{O_2})

only when the pulmonary artery minus left atrial mean pressure is used for calculating the total pulmonary resistance. There is steady control of output, and the usefulness of the constant level well is seen. Data on the 3 animals carried through the nine-stage experiment, as seen in Table I and Fig. 4, show these same phenomena. Examples of the lack of correlation between decrease in inspired oxygen concentration on the resistance change in these circumstances can also be seen.

With such a complex experiment, a number of monitors and controls were instituted to keep as stable a preparation as possible. If a heat exchanger were not in the system, the temperature fell to 29° to 31° C.; therefore, the heat exchanger in the circuit is mandatory. Temperature measurements at the blood, muscle, and rectal sites indicated stability at 36° to 38° C. in all experiments. At least two electrolyte checks were obtained and little change found. Repeated acid-base studies indicated no profound abnormality—a mild, metabolic acidosis was occasionally present, as is often associated with surgical procedures and anesthesia, and a respiratory alkalosis was usually present, often compensating the acidosis, reflecting not only hyperventilation but decarboxylation by the bubble oxygenator. Whole blood hematocrit measurements changed little throughout the procedure. There were occasional instances of pulse abnormality. In 1 animal not used for this study, there was a period of bradycardia just before going on bypass, and calculated resistance did not vary, whereas changes occurred in cardiac output and phasic pulmonary artery pressure because of this bradycardia. These data are as follows:

Pulse—48/min.
P.A. = $27/5\ \overline{12}$ mm. Hg
$PA_m - LA_m = 10$ mm. Hg
C.O. = 1.96 L./min.
2.19 L./min.
R = 408 dyne sec. cm.$^{-5}$
365 dyne sec. cm.$^{-5}$

Pulse—78/min.
P.A. = $22/15\ \overline{17}$ mm. Hg
$PA_m - LA_m = 13$ mm. Hg
C.O. = 2.47 L./min.
R = 421 dyne sec. cm.$^{-5}$

Right ventricular pressure was used to monitor ventricular diastolic pressure for evidence of failure; however, when a marked change occurred, the cannula pulled back into the right atrium (see Fig. 3) and, as noted in Table I, an occasionally unusable pressure curve was obtained. In rare instances, an acute, but temporary, elevation of the diastolic pressure was found as in the second experiment of Table I. During the times of marked increase in pulmonary vascular resistance, there is a modest increase in the diastolic pressure reflected in the right atrial pressure. Furthermore, the systolic level of the right ventricular pressure served as a check on the systolic level in the pulmonary artery, the most important pressure parameter.

A portion of lung was biopsied from each side at the end of the procedure to check for thromboses, arterial abnormalities, worms, etc. The heart and major proximal vessels were opened and examined grossly for the same reasons. None was noted.

DISCUSSION

The oxygenation of the pulmonary artery blood under these circumstances is 30 to 60 per cent above that of the usual mixed venous oxygen saturation, and from a pulmonary circulatory point of view, it is therefore hyperoxic. Smith,[23] Bennett[24] and their associates, in 1932-1934, demonstrated pathologic pulmonary arterial changes and elevation of pulmonary artery pressure in rats when the animals were subjected to chronic elevation of atmospheric pressure, and it is notable that the environmental oxygen tension was 635 mm. Hg. They felt that the pulmonary hypertension may have been present early but had not been measured. It is clear that one of the next steps in this study is to control the oxygenation and to measure Po_2, as well as the oxygen saturation, especially when saturations of 100 per cent oxygen are obtained.

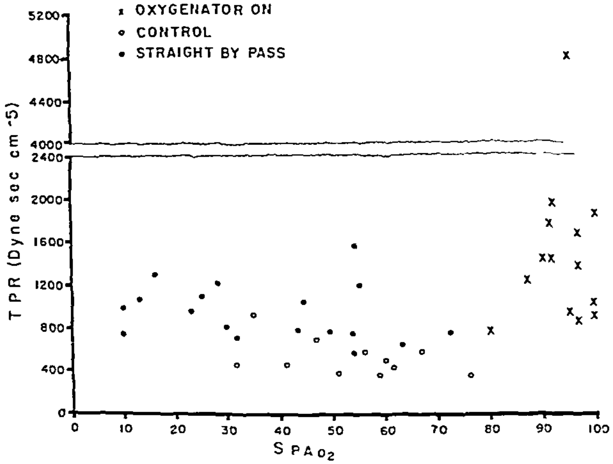

Fig 6—Plot of values of pulmonary arterial oxygen saturation ($SPAo_2$) and calculated total pulmonary resistance (TPR) (when obtained simultaneously) under the three experimental circumstances (control bypass and oxygenator) in an attempt to elucidate the effect of hypoxia as well as hyperoxia on vascular resistance

How does this hyperoxic reaction relate to shunts? At the present time an extensive survey is being done on our own and published catheterization data to see if there is any relationship between the measured pulmonary arterial oxygen saturation and the measured pulmonary vascular resistance, however, it would seem that there is not such a correlation. For example, the large interatrial septal defects are commonly associated with a high value of mixed venous oxygen saturation and, in general, are usually associated with normal or low pulmonary vascular resistances. On the other hand, small shunts from the high pressure circuit in ventricular septal defect and patent ductus can be associated with increased vascular resistance. The direct pressure effect, jet effect, laminar flow of hyperoxygenated blood (otherwise well mixed from an atrial side), striking pulmonary receptors from a high pressure source, or some other factor may be operating.

In many instances the presence of the bypass itself, without the bubble oxygenator in the system, was associated with increased pulmonary vascular resistance. However, two things must be noted. The bypass is initiated with an oxygenated blood drawn from the donors' arterial systems and, in two instances, measurement of the saturation has shown it to be high. For example, in the dog with the reversible bypass, the initial institution of bypass was associated with a donor blood oxygen concentration of 91 per cent and there was a striking increase in pulmonary arterial pressure, cardiac output, and resistance. As time progressed and the saturation fell to 67 per cent, there was a return toward normal, but not to normal, of these circulatory dynamics. Reverse of the bypass to control produced a normal pattern; then reinstitution of the bypass from a circuit now containing venous oxygenated blood of close to 60 per cent produced little or no change in resistance and only a slight increase in output and pressure. Addition of the oxygenator, inducing a pulmonary artery blood oxygen concentration of 100 per cent, produced a marked increase in pulmonary vascular resistance. Bypass alone produced reversion of vascular resistance close to normal. Return to normal circulation reproduced control resistances, although associated with a somewhat lower cardiac output.

Could there be a bifid reaction; that is, a modest stimulus to increased vascular resistance from decreased oxygen concentration and a marked stimulus with increased oxygen concentration? Fig. 6 shows a plot of data in which a pulmonary arterial oxygen saturation was obtained at the same time as total pulmonary resistance was calculated and, as can be seen with the three groups of studies—control, straight bypass, and bypass with oxygenator—there is a tendency to a somewhat increased resistance at the lower oxygen concentration and a clear-cut indication of increased resistance at high oxygen concentrations. There is too much scatter and too few points to judge the hypoxic effect, especially in view of the variation in circumstances of measurement.

There are certain clinically useful suggestions from this study. In the pulmonary hypertensive patients undergoing extracorporeal circulation in whom the lungs fill with blood from the systemic side of the circuit and are usually ventilated with gas of high oxygen concentration, the stage for a further increased pulmonary vascular resistance, obtainable at the time of coming off of bypass, might be set, and some variation in the inhaled gas mixture might be worthy of study. The possible deleterious effect of small shunts, and especially small residual post-surgical shunts in patients with pulmonary hypertension, may assume great significance.

The increased pulmonary vascular resistance under hypothermia might also be explained by this mechanism, as the oxygen saturation of mixed venous blood increases as a result of decreased peripheral metabolism and arteriovenous shunting.

SUMMARY

Observations with the use of a controlled extracorporeal shunt from venae cavae to right atrium in which the oxygenation of the blood, other than that returning by the coronary sinus, can be controlled, have shown an increased vascular resistance associated with the institution of the bypass circuits and, most importantly, a striking increase in all parameters related to increased *total*

pulmonary resistance and pulmonary hypertension when excessively oxygenated blood is returned to the right side of the heart The vascular reaction to oxygenated blood in the pulmonary circuit has even been lethal in normal dogs.

The technical assistance of Florence Kosmal and William Rank is gratefully acknowledged

REFERENCES

1 Von Euler, U. S, and Liljestrand, G.: Observations on the Pulmonary Arterial Blood Pressure in the Cat, Acta physiol. scandinav. 12: 301, 1946
2 Motley, H L., Cournand, A., Werko, L, Himmelstein, A., and Dresdale, D.: The Influence of Short Periods of Induced Acute Anoxia Upon Pulmonary Artery Pressures in Man, Am. J. Physiol. 150: 315, 1947.
3 Westcott, R N., Fowler, N. O., Scott, R C., Harrenstein, V. D., and McGuire, J: Anoxia and Human Pulmonary Vascular Resistance, J. Clin. Invest. 30: 957, 1951
4 Fishman, A P, McClement, J., Himmelstein, A., and Cournand, A: Effects of Acute Anoxia on the Circulation and Respiration in Patients With Chronic Pulmonary Disease Studied During the "Steady State," J. Clin. Invest. 31: 770, 1952
5 Doyle J. T., Wilson, J. S, and Warren, J. V.: The Pulmonary Vascular Responses to Short Term Hypoxia in Human Subjects, Circulation 5: 263, 1952
6 Duke, H. N: The Site of Action of Anoxia on the Pulmonary Blood Vessels of the Cat, J. Physiol 125: 373, 1954
7. Aviado, D M, Ling, J. S, and Schmidt, C F.: Effects of Anoxia on Pulmonary Circulation: Reflex Pulmonary Vasoconstriction, Am. J. Physiol. 189: 253, 1957.
8 Lewis, B M, and Gorlin, R. Effects of Hypoxia on Pulmonary Circulation of the Dog, Am. J. Physiol. 170: 574, 1952
9 Stroud, R. C., and Rahn, H.: Effect of O_2 and CO_2 Tensions Upon the Resistance of Pulmonary Blood Vessels, Am J Physiol 172: 211, 1953
10 Heemstra, H: The Development of an Increased Pulmonary Vascular Resistance by Local Hypoxia, Quart. J. Exper Physiol. 39: 83, 1954
11 Nahas, G G, Visscher, M. B., Mather, G. W., Haddy, F. J, and Warner, H. R.: Influence of Hypoxia on the Pulmonary Circulation of Nonnarcotized Dogs, J. Appl Physiol 6: 467, 1954
12 Lanari Zubiaur, F. J., and Hamilton, W F.: Effect of Unilateral Anoxia on Pulmonary Circulation, Circulation Res 6: 289, 1958.
13 Rodbard, S, and Harasawa, M: The Passivity of the Pulmonary Vasculature in Hypoxia, Am Heart J. 57: 232, 1959
14 Smith, D. J, and Coxe, J. W: Reactions of Isolated Pulmonary Blood Vessels to Anoxia, Epinephrine, Acetylcholine and Histamine, Am. J. Physiol 167: 732, 1951
15 Ferguson, D. J., Berkas, E M., and Varco, R L: Circulatory Factors Contributing to Alterations in Pulmonary Vascular Histology, S Forum Am College Surgeons 4: 267, 1953
16 Ferguson, D J, Berkas, E M, and Varco, R. L: Experimental Methods for the Production of Pulmonary Hypertension *in* Pulmonary Circulation, edited by W Adams, and I. Veith, New York, N Y, 1959, Grune & Stratton, pp 126 137.
17 Muller, W. H, Dammann, J F, and Head, W H. Changes in the Pulmonary Vessels Produced by Experimental Pulmonary Hypertension, Surgery 34: 363, 1953
18 Lancaster, J. R, Harrison, R W, Gold, R, and Moulder, P V: Effect of Systemic—Right Atrial Shunts on the Pulmonary Circulation (To be published)
19 Boake, W. C, Daley, R, and McMillan, I K. Observations on Hypoxic Pulmonary Hypertension, Brit Heart J 21. 31, 1959
20 Rattenborg, C: Anestesiventil: Ventil til cirkelsystem og kunstig ventilation uden genånding, Ugesk. læger 118: 1168, 1956
21 Moulder, P. V, Eichelberger, L E, and Roma, M: Histochemical Characterization of Heart and Skeletal Muscle During Growth, A M A Arch Surg 75: 165, 1957
22 Peters, J. P, and Van Slyke, D D Quantitative Clinical Chemistry (Methods), Baltimore, 1931, Williams & Wilkins Co, vol 2
23 Smith, F. J C, Bennett, G A, Heim, J W, Thompson, R M, and Drinker, C. K: Morphological Changes in the Lungs of Rats Living Under Compressed Air Conditions, J Exper Med. 56. 79, 1932
24 Bennett, G A, and Smith, F. J C: Pulmonary Hypertension in Rats Living Under Compressed Air Conditions, J Exper Med 59: 181, 1934

(*For Discussion, see page 631*)

TREATMENT OF BANK BLOOD BY RESINS

Edward D. McLaughlin, M.D. (by invitation), Thomas F. Nealon, Jr., M.D., and John H. Gibbon, Jr., M.D., Philadelphia, Pa.

The successful application of cation exchange resins to reduce abnormally high levels of ammonium and potassium in stored blood has been reported by Schechter, Nealon, and Gibbon.[6] Blood so treated still has an abnormally low pH, chiefly because of citrate preservative. By passing bank blood over an anion exchange resin, McLaughlin, Nealon, and Gibbon[4] were able to return pH and elevated anion concentrations to normal by substituting bicarbonate for the citrate and other increased anions.

The successful use of extracorporeal circulation in the treatment of various diseases in human beings has necessitated obtaining large quantities of compatible blood to prime the apparatus. Blood for this purpose is usually drawn within 24 hours of the scheduled time of operation. A number of previously typed and crossmatched donors therefore have to assemble at one time and place to donate this priming blood. If stored bank blood could be safely used, the collection of blood for open-heart operations would be greatly facilitated. The purpose of this study was to determine whether the electrolyte concentrations of canine bank blood could be restored to approximately normal values by passage over both an anion and a cation exchange resin. The safety of using this resin-treated blood was then tested by means of exchange transfusions in normal dogs.

METHODS AND MATERIALS

Donor blood was obtained by exsanguinating healthy adult mongrel dogs. ACD solution, Formula A, 75 ml. per 480 ml. of whole blood, was employed as the preservative. The 75 ml. of Formula A contains 1.64 Gm. trisodium citrate, 0.6 Gm. citric acid, and 1.84 Gm. dextrose (USP). Eight donor pools, each containing 3,000 ml. of whole blood, were stored in siliconized, sterile bottles at 5° C. Each pool was composed of blood from 3 or 4 different dogs. Four pools were stored for 14 days, and 4 for 21 days. A heparinized sample of blood from each dog was analyzed for blood pH, plasma hemoglobin, and

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Read at the Fortieth Annual Meeting of The American Association for Thoracic Surgery at Miami Beach, Fla., May 11-13, 1960.

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Potassium.—Potassium concentration in plasma of bank blood increased progressively to an average of 17 mEq./L. after 14 days and 22 mEq./L. after 21 days of storage. After passage over the cation exchange resin the markedly elevated levels were reduced to less than 1.0 mEq./L.

Calcium.—The addition of ACD solution reduced the plasma calcium level, as measured by the technique employed, to approximately 25 per cent of normal. Since the calcium was not removed it must have been bound in unmeasurable form by the citrate. After the removal of the citrate by the anion exchange resin the calcium concentration was only 50 per cent of the original level. The present data do not account for the remainder of the calcium.

Ammonium.—Blood ammonium content increased progressively during storage so that after 3 weeks the concentration had approximately tripled. Reduction to the normal range occurred after passage over the cation exchange resin.

Citrate.—When ACD solution was added to fresh blood the plasma citrate concentration rose from an insignificant amount to approximately 450 mg. per 100 ml. The concentration did not change during storage. Passage of the blood over the anion exchange resin reduced the citrate content to normal.

Phosphate.—The phosphate concentration in the plasma after storage was about double that in fresh blood. After passage over the anion resin, the concentration returned to the normal range.

Lactate.—The lactate content of the blood rose markedly during storage. Passage over the anion resin removed the greater part of this increase, but did not reduce the concentration of lactate to the normal range.

Pyruvate.—After storage, the pyruvate content of blood was five or six times the pre-storage level. After traversing the anion resin, the pyruvate concentration returned to normal.

Plasma Hemoglobin.—During storage there was an increase in plasma hemoglobin. Passage of the blood over both resin columns resulted in slight increases in plasma hemoglobin.

To recapitulate, the addition of ACD solution to blood produced some increase in plasma sodium, a large increase in citrate with a concomitant decrease in ionizable plasma calcium and a marked drop in pH. With storage there was an increase in ammonium, potassium, phosphate, lactate, and pyruvate, and a decrease in plasma chloride with a further drop in pH. After passage over the resins the electrolyte concentrations returned to normal values except for potassium, calcium, and chloride (which were low), and lactate (which was high). There was a marked rise in pH due to the removal of the citrate and accumulated anions.

Eight dogs were given exchange transfusions of the resin-treated blood. None showed ill effects from the transfusion. When the animals were sacrificed 14 days after the exchange transfusion, postmortem examination showed no gross evidence of infection, hemorrhage, thrombosis, emboli, or infarction.

TABLE I. CHANGES IN CANINE BLOOD STORED AT 5° C. FOR 14 DAYS
(AVERAGE OF 4 POOLS OF BLOOD OF 3 L. EACH)

	pH BLOOD	Na PLASMA (MEQ./L.)	Cl PLASMA (MEQ./L.)	K PLASMA (MEQ./L.)	Ca PLASMA (MG./100 ML.)	NH_4 BLOOD (MCG./100 ML.)	CITRATE PLASMA (MG./100 ML.)	PO_4 PLASMA (MG./100 ML.)	LACTATE BLOOD (MG./100 ML.)	PYRUVATE BLOOD (MG./100 ML.)	Hb PLASMA (MG./100 ML.)
Blood											
0 Day											
Heparin	7.37	146	117.9	4.1	9.6	136.6	1.7	3.76	26.6	1.66	9.06
After addition ACD solution	6.83	164	100.8	3.5	2.5	117.8	131.6	3.15	24.2	1.50	14.5
14 Day											
Storage at 5° C.	6.17	168	80.7	16.9	1.9	367.5	442.4	7.52	155.3	7.73	62.0
After passage over resins	7.07	136	82.9	0.3	4.5	116.5	3.5	2.52	58.6	0.8	70.1

TABLE II. CHANGES IN CANINE BLOOD STORED AT 5° C. FOR 21 DAYS
(AVERAGE OF 4 POOLS OF BLOOD OF 3 L. EACH)

	pH BLOOD	Na PLASMA (MEQ./L.)	Cl PLASMA (MEQ./L.)	K PLASMA (MEQ./L.)	Ca PLASMA (MG./100 ML.)	NH_4 BLOOD (MCG./100 ML.)	CITRATE PLASMA (MG./100 ML.)	PO_4 PLASMA (MG./100 ML.)	LACTATE BLOOD (MG./100 ML.)	PYRUVATE BLOOD (MG./100 ML.)	Hb PLASMA (MG./100 ML.)
Blood											
0 Day											
Heparin	7.33	136	117.2	4.1	9.2	133.8	1.3	3.64	10.9	1.08	10.6
After addition ACD solution	6.72	160	101.4	3.9	1.26	128.2	161.4	3.46	10.3	0.98	17.5
21 Day											
Storage at 5° C.	6.14	160	80.6	22.0	1.38	155.3	156.6	7.05	159.1	6.8	35.9
After passage over resins	7.14	137	81.9	0.9	1.7	136.3	1.6	3.07	68.8	17.3	52.6

Blood analyses in a typical experiment in which a dog was given an exchange transfusion of pooled blood stored for 2 weeks are shown in Table III. The same studies in another animal given exchange transfusion of blood stored for 3 weeks are shown in Table IV. Part of these changes are shown graphically in Fig. 1.

The changes in these individual pools of blood are similar to the average changes listed in Tables I and II. The recipient dog's blood prior to transfusion was similar to the freshly drawn heparinized pooled blood. The stored pooled ACD blood after it was treated by resins had a low potassium, calcium, and chloride, and an elevated lactate with a resultant low pH. Two hours after transfusion all values were similar to those of the dog before transfusion except the lactate which was elevated but lower than in the pooled blood. Twenty-four hours after transfusion all values were normal.

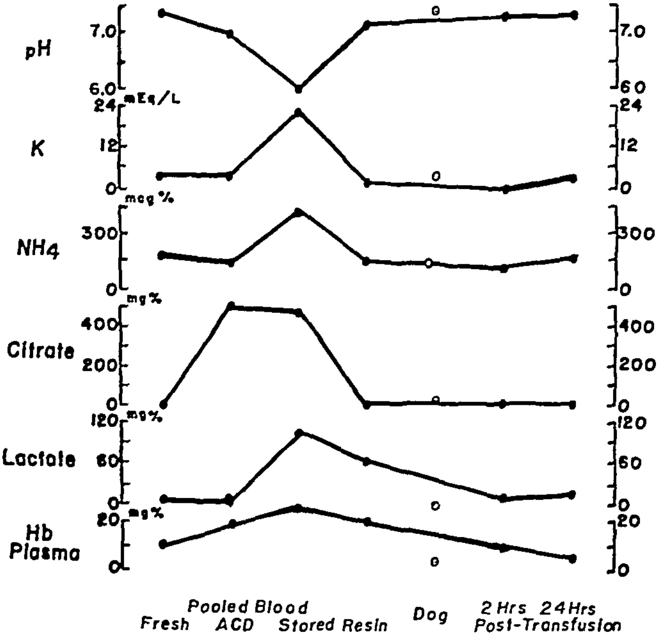

Fig 1 —Changes which occurred in pH potassium, ammonium, citrate, lactate, and plasma hemoglobin during storage for 21 days, passage over resins, and after exchange transfusion The open circles are the levels in the blood of the recipient dog.

DISCUSSION

ACD solution is used to preserve blood in almost all blood banks. The blood stored in ACD solution in glass bottles is generally discarded after 21 days' storage at 5° C. Less than 70 per cent of the cells retain full functional capacity after infusion if such blood is stored for longer periods. If ACD blood is stored in plastic containers, 70 to 80 per cent viability has been demonstrated after 25 days.[7]

TABLE III. POOL "D" FOR EXCHANGE TRANSFUSION WITH DOG "D"

	pH BLOOD	Na PLASMA (MEQ./L.)	Cl PLASMA (MEQ./L.)	K PLASMA (MEQ./L.)	Ca PLASMA (MG./100 ML.)	NH_4 BLOOD (MCG./100 ML.)	CITRATE PLASMA (MG./100 ML.)	PO_4 PLASMA (MG./100 ML.)	LACTATE BLOOD (MG./100 ML.)	PYRUVATE BLOOD (MG./100 ML.)	Hb PLASMA (MG./100 ML.)
Blood											
0 Day											
Heparin	7.38	153	118.8	3.6	10.0	149.3	2.4	3.87	31.0	1.57	8.2
After addition ACD solution	6.81	163	108.6	3.6	2.2	141.2	430.3	3.21	28.8	1.52	19.7
14 Day											
Storage at 5° C.	6.16	175	88.6	16.8	2.1	371.5	435.8	8.23	186.7	4.25	52.5
After passage over resins	7.11	139	94.2	0.3	4.5	139.0	3.5	2.3	65.2	0.36	67.4
Dog D											
Before transfusion	7.30	167	122.9	4.2	9.1	137.7	1.8	3.63	23.0	1.06	19.9
2 hr. after transfusion	7.31	153	110.2	3.4	8.5	145.3	2.4	3.87	55.2	2.20	49.9
24 hr. after transfusion	7.34	147	118.8	3.6	10.0	149.8	3.5	3.52	31.0	0.57	8.21

Blood stored in citrate-phosphate-dextrose (CPD) solution was studied by Gibson, Rees, McManus and Scheitlin in 1957.[2] They reported more than 70 per cent viability of infused cells after 28 to 32 days' storage at 4° C. when the blood was contained in a plastic bag and infused in plastic recipient sets. A recent report indicates that multiple transfusions of such blood can be given to human beings without significantly elevating the plasma phosphate levels.[3] The CPD solution has the further advantage that it alters the pH less than does the ACD solution. It drops the pH to about 7.2 as compared to 6.8 to 7.0 with ACD solution. Previous work in this laboratory demonstrated that there is an even greater accumulation of potassium and ammonium when CPD solution is used. However, passage over a cation exchange resin will remove the excess potassium and ammonium.

Heparinized blood used to prime heart-lung machines is collected within 24 hours of operation. After 48 hours, heparinized blood tends to develop tiny clots. ACD-preserved blood with its high concentrations of potassium, ammonium, and citrate cannot be used. Smith, Brown, Young, and Sealy[7] have successfully primed a heart-lung machine with blood stored up to 5 days using Edglugate Mg as a preservative. Beyond that time, increased potassium and depression of antihemophilic globulin and factor V levels contraindicate its use.

Since our animals tolerated exchange transfusions of ACD blood treated by ion exchange resins with no ill effects, it is possible that such blood might prove satisfactory for priming heart-lung machines. Stored blood so treated must be tested in the extracorporeal apparatus to determine the period of storage permissible for animals and for man. If it proves safe to use ordinary bank blood for this purpose, collection of blood for open cardiac operations would be greatly simplified. Furthermore, bank blood would be available for emergency use of the heart-lung machine.

SUMMARY

1. Altered levels of blood pH and metabolites and of plasma electrolytes which are present in stored ACD blood may be restored to approximately normal values after passage over anion-cation exchange resins.

2. Canine ACD blood stored 2 to 3 weeks and then treated by anion-cation exchange resins and used for exchange transfusions in dogs produced no detectable harmful effects to the recipients.

REFERENCES

1. Challet, H. A., Clauss, R. H., Giannini, S. G., and MacFee, W. F.: A Safe and Simple Method of Blood Collection for Transfusion Utilizing a Cation Exchange Resin. Ann. Surg. 147: 69-74, 1958.
2. Gibson, J. G., II, Rees, S. B., McManus, T. J., and Scheitlin, W. A.: Citrate-Phosphate-Dextrose Solution for Preservation of Human Blood. Am. J. Clin. Path. 28: 569-578, 1957.
3. Gibson, J. G., II, Rees, S. B., and McManus, T. J.: Replacement of Blood Loss During Surgical Procedures With Blood Collected in Citrate Phosphate Dextrose Solution. New England J. Med. 262: 595-597, 1960.

TABLE IV. POOL "F" FOR EXCHANGE TRANSFUSION WITH DOG "F"

	pH BLOOD	Na PLASMA (MEQ./L.)	Cl PLASMA (MEQ./L.)	K PLASMA (MEQ./L.)	Ca PLASMA (MG./100 ML.)	NH_4 BLOOD (MCG./100 ML.)	CITRATE PLASMA (MG./100 ML.)	PO_4 PLASMA (MG./100 ML.)	LACTATE BLOOD (MG./100 ML.)	PYRUVATE BLOOD (MG./100 ML.)	Hb PLASMA (MG./100 ML.)
Blood											
0 Day											
Heparin	7.36	139	108.3	4.1	9.7	147.9	1.2	3.8	9.2	1.07	10.6
After addition ACD solution	6.91	158	90.3	4.0	0.9	143.9	453.0	3.6	9.0	1.01	19.1
21 Day											
Storage at 5° C.	6.01	161	75.1	22.1	1.1	437.6	447.9	6.5	109.2	6.5	24.2
After passage over resins	7.14	130	77.5	1.5	3.9	145.9	1.2	3.4	60.5	1.8	21.8
Dog F											
Before transfusion	7.38	144	116.6	3.9	8.9	143.3	2.4	4.27	5.0	1.22	4.7
2 hr. after transfusion	7.30	139	108.3	4.1	8.3	137.9	1.4	3.80	9.2	1.07	10.6
24 hr. after transfusion	7.36	147	123.0	3.4	9.3	148.8	1.3	4.14	22.2	1.22	5.9

GAS-EXCHANGE DYNAMICS OF GLYCEROLIZED FROZEN BLOOD

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Clinical experience has demonstrated to us that blood treated with glycerol and stored for prolonged periods of time in the frozen solid state may be used, on thawing, as a satisfactory total blood volume replacement during cardiovascular surgery and extracorporeal circulation.[18] This finding has resulted in a considerable improvement in the logistics of blood procurement and increased flexibility in tailoring blood transfusion requirements to the needs of the individual patient.

Basic studies of the glycerolization technique by Tullis and associates of the Protein Foundation, Inc., demonstrated that human red blood cells could be stored at -80 or -120° C. for periods up to 44 months.[24, 25] When such cells were thawed and transfused, their survival in the circulation was comparable to that of freshly drawn cells treated by conventional blood bank techniques. Prior to the freezing process, it was necessary to separate cells from plasma and to treat the cellular elements of the blood with glycerol to minimize the formation of large ice crystals (which might disrupt the cell membrane) to prevent increased ionic concentrations within the cell as water was transformed to ice, and to minimize extracellular diffusion of important cell constituents.[1, 14, 21] After thawing, the glycerol was removed from the cells by washing and the cells were reconstituted in their own plasma or a suitable suspension medium containing purified albumin solution. The various manipulations of cell separation and introduction and removal of glycerol from the cells require a modification of the fractionating centrifuge originally devised by Cohn for separation of cellular and protein fractions of fresh blood (Fig. 1).[2, 24, 25] Since glycerol, the cellular elements of the blood, and the various plasma components have varying specific gravities, centrifugation affords a method for separating blood elements or for the introduction or removal of glycerol from the separated cellular elements. Cell destruction is minimal during processing and the closed system ensures complete asepsis.

From the Blood Preservation and Surgical Research Laboratories of the U. S. Naval Hospital, Chelsea, Mass., the Department of Surgery, Lahey Clinic, and the Surgical Service, New England Deaconess Hospital, Boston, Mass.

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4. McLaughlin, E. D., Nealon, T. F., Jr., and Gibbon, J. H, Jr.: The Removal of the Citrate Additive and Accumulated Anions From Bank Blood (To be published)
5. Sack, T., Gibson, J. G., and Buckley, E. S., Jr.: The Preservation of Whole ACD Blood Collected, Stored, and Transfused in Plastic Equipment, Surg. Gynec & Obst 95 113 119, 1952.
6. Schechter, D. C., Nealon, T. F, Jr, and Gibbon, J. H, Jr.: The Removal of Excessive Potassium and Ammonium From Bank Blood Prior to Transfusion, Surg Gynec & Obst. 108: 1 6, 1959.
7. Smith, W. W., Brown, I. W., Jr., Young, W. G, Jr., and Sealy, W. C: Studies of Edglugate Mg: A New Donor Blood Anticoagulant-Preservative Mixture for Extracorporeal Circulation, J THORACIC SURG. 38: 573 585, 1959.

(For Discussion, see page 631)

citrate-dextrose solution. In view of this experience it seemed advisable to test blood passed through the glycerolization process as replacement in the massive amounts required so frequently for cardiac and thoracic surgery. Such a study was given added impetus by the finding in our laboratory that heparinized blood treated by the glycerolization process maintains full heparin activity up to 7 months' storage at –80° C. (the longest period studied).[19] It seemed possible that heparinized blood could be stock-piled without time limitation and then used as a medium for pump-oxygenator priming and transfusion during open-heart or vascular surgery.

Basic to such an application was the need for confirmation of the clinical observation that glycerolization did not alter hemoglobin structure or intracellular environment so that the ability of the red blood cell to transport gases was seriously impaired. Certain properties of oxygen transport by the red blood cell are expressed by the oxyhemoglobin dissociation curve, which equates values of oxyhemoglobin saturation (the percentage of total hemoglobin in the oxygenated state) to the partial pressure of oxygen in a gas mixture in equilibrium with the blood. Construction of an oxyhemoglobin dissociation curve for a given blood specimen enables one to draw conclusions as to the manner in which that blood will give up oxygen within the tissues to provide an oxygen pressure within the tissues for adequate aerobic cellular metabolism.

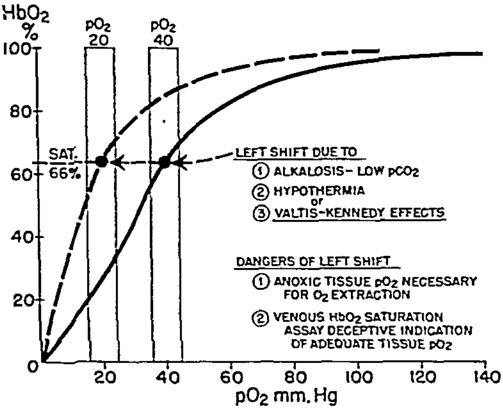

Fig 2.—Diagrammatic representation of consequences of a shift to the left of the normal oxyhemoglobin dissociation curve (*solid line*).

Of particular significance in the present study was the finding by Valtis and Kennedy[27] that blood collected in the usual acid-citrate-dextrose solution demonstrated an impairment of oxyhemoglobin dissociation after a number of days' storage at 4° C. The character of the changes demonstrated by them are illustrated diagrammatically in Fig. 2. As a result of a shift to the left of the oxyhemoglobin dissociation curve, the tissue oxygen concentration or partial pressure (pO_2) is in danger of falling to anoxic levels before an adequate dissociation of oxygen from hemoglobin may occur.

The curve shift gradually reversed once the transfused blood was within the body, but large volume blood replacements resulted in serious impairment

In 1956, The Blood Preservation Laboratory was established at the U. S. Naval Hospital, Chelsea, Massachusetts, to evaluate the merits of the glycerolization-freezing method at a clinical level.[22] Haynes and associates[7] soon established the value of the method in over 1,000 transfusions. In addition to the obvious advantages of blood stock-piling without the necessity for discarding outdated blood, the over-all reaction rate was found to be only one tenth of that seen following conventional transfusion of blood preserved at 4° C. in acid-

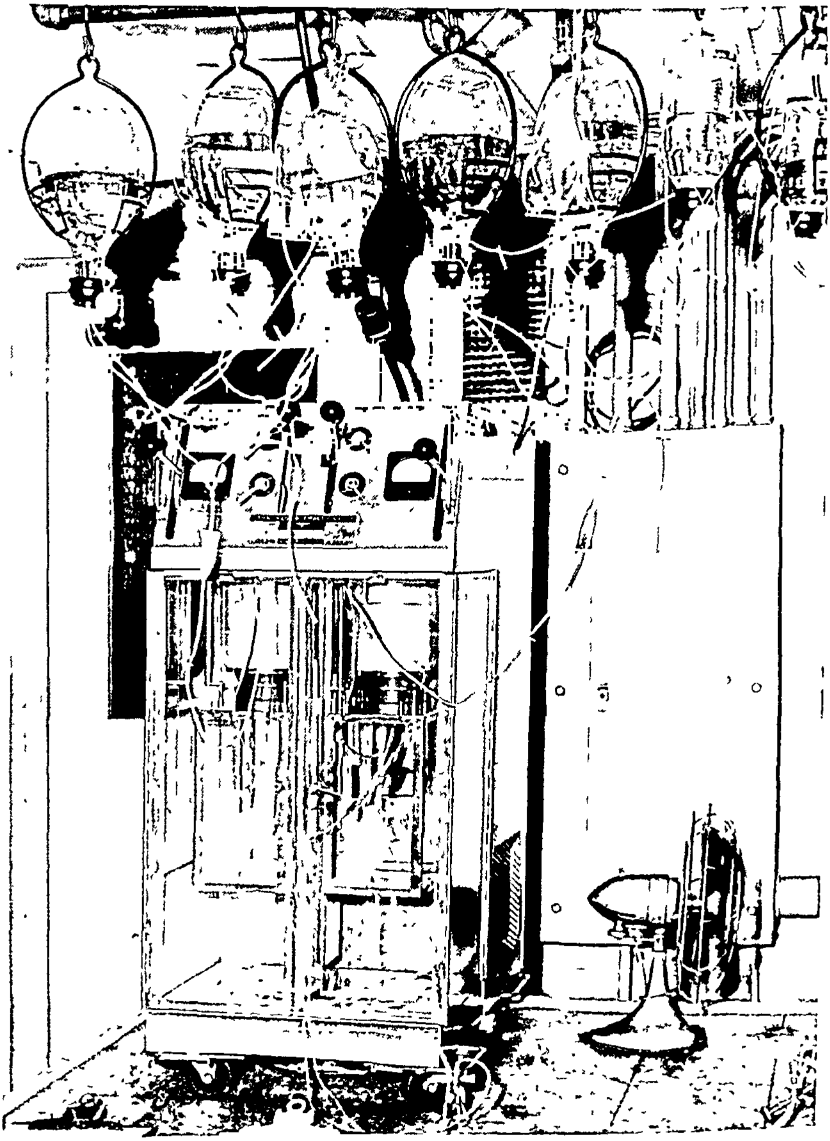

Fig 1.—View of the Cohn A. D L blood fractionator during glycerolization of blood. Wash solutions are suspended above the unit The interchangeable sterile cartridge unit bearing the rotating centrifuge bowl and collection bags is located within a refrigerated compartment. The centrifuge bowl connects to the drive mechanism by a chuck attachment. Drive controls are located above the spinning bowl.

interchangeable cartridge unit, the dangers of contamination during attachment of tubing connections are eliminated.

In the glycerolization phase, blood is forced onto the rotating bowl at a flow rate of approximately 50 ml. per minute. The bowl is rotated to give a gravitational force of 425 g. The blood passes to the periphery of the bowl by centrifugal force. Separation of the blood into a heavier red cell layer at the bowl periphery and an inner lighter plasma layer occurs as the bowl fills to its capacity of 350 ml. The separated plasma accumulates in the inner area of the bowl and overflows a central weir into a plastic bag. After the entire unit of blood has been infused and the maximal amount of plasma collected, the plasma bag is sealed and detached from the cartridge unit for freezing. Without interruption, a large volume of 20 per cent solution of glycerol is introduced into the bowl followed by a large volume of 50 per cent glycerol. As each successive glycerol solution increases in volume within the centrifuge, it traverses the packed cell residue contained within the bowl from the periphery to the central weir of the bowl and thence spills over into a discard outlet. The plasma remaining in the bowl at the end of the cell separation cycle dilutes the initial portions of 20 per cent glycerol entering the bowl and a similar dilution occurs as the glycerol solution concentration is increased. Glycerol equilibration between the cells and wash solution thereby progresses gradually by means of counter-current dialysis. Following addition of the 50 per cent glycerol solution, the centrifuge is stopped, permitting the glycerolized cells to flow into a separate plastic bag which is sealed and detached.

The plasma and red cell bags are marked and placed in a cardboard container for storage in a −80° or −120° C. freezing unit. Temperatures prevailing within the freezers are continuously recorded. An automatic alarm system signals any possible failure of the freezer mechanism. Temperature equilibration is obtained within 6 to 8 hours after the bags are placed within the freezer.

To reconstitute the blood, the frozen units are thawed for 10 minutes in a rotating water bath at 37° C. Glycerol is removed from the cell mass by exposure within the centrifuge to solutions containing decreasing concentrations of glycerol. This dialysis must progress gradually since water will enter the cell four times faster than the glycerol will leave and a slow step-wise progression must be used to prevent hemolysis. A small amount of plasma is washed through to displace the last wash solution. The cell mass is then removed into a plastic administration bag where it can be reconstituted with its own plasma or other desired suspension medium. The reconstituted blood is stored at 4° C. until ready for use.

It now takes us 35 minutes to glycerolize a unit of blood and 45 minutes to reconstitute it. With the present equipment one technician can process four units simultaneously. Glycerol concentration is 40 per cent within the frozen cell and less than 1 per cent following reconstitution. To meet special clinical requirements, the electrolyte concentration and pH of the reconstituted blood may be varied at will by altering the composition of the final washing solutions.

Blood and Gas Analysis Methods.—

Blood samples were withdrawn from patients by arterial or venous puncture. During *in vitro* studies, plastic blood bags were inverted 25 times to assure adequate mixing. Blood was withdrawn for sampling or stored after equilibration in Luer-Lok syringes lightly lubricated with mineral oil. Syringe dead space was filled with 1 per cent heparin solution in saline. Following collection of a sample, the syringe was sealed with mercury, capped with a locking hub, and immediately immersed in an ice bath.

Samples of blood 6.0 ml. in volume were equilibrated in Barcroft tonometers of approximately 325 ml. capacity by rotation for 20 minutes in a 37° C. water bath, following gassing of the tonometer for 30 seconds at 3 L. per minute from cylinders containing varying proportions of nitrogen, oxygen, and carbon dioxide. The carbon dioxide tension was approximately 40 mm. Hg in each cylinder and the ratio of nitrogen to oxygen varied to give approximate oxygen tensions of 15, 25, 30, 60, 90, or 120 mm. Hg.

of tissue oxygen tension persisting for several days At certain times, the tissue oxygen tension could be actually worsened by transfusion despite apparent correction of an anemic state. The implications of such a situation are obvious in thoracic surgery, where the derangement may be compounded by diminished cardiac output and ventilatory reserve.

The Valtis-Kennedy effect is related to variations of blood electrolyte concentrations and may be eliminated by addition of sodium chloride to plasma[26] Since the glycerolization process (unless carefully controlled) might be expected to derange just these electrolyte concentrations, a determination of oxyhemoglobin dissociation properties was necessary to confirm our impression that a serious alteration of hemoglobin chemistry was not induced by the glycerolization process.

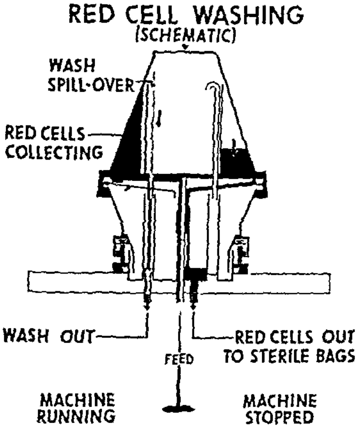

Fig 3.—Diagrammatic representation of the centrifuge bowl used for cell separation and washing.

METHODS

Glycerolization and Freezing of Blood.—

Blood from a healthy young donor is collected by phlebotomy, drawing 475 ml. into a plastic bag containing either acid citrate dextrose solution or heparin saline solution. The citrate bag contains 75 ml of acid citrate dextrose solution, National Institutes of Health Formula A. The heparin bag contains 2,000 USP units of heparin sodium in 30 ml of 0 89 per cent sodium chloride solution buffered to pH 7.4 Between collection and glycerol processing, the bags are stored at 4° C. for periods up to 5 hours

Blood is glycerolized and deglycerolized by passage through a centrifuge of the Cohn type (Cohn A.D.L fractionator*) (see Fig. 1). Interchangeable cartridge units are placed within a refrigerated compartment of the fractionator and the centrifuge portion of the cartridge assembly rotated at a revolution rate which may be varied depending upon the type of separation desired. A diagram of the Type II centrifuge bowl (Fig. 3) used for glycerolization and deglycerolization illustrates the manner of introduction of blood and withdrawal of blood fractions. Blood or washing solutions are admitted by pressure flow through a plastic tube manifold. After passage through the centrifuge bowl, the separated elements are collected in plastic bags connected to outlet ports in the base of the bowl. Since the collecting bags and centrifuge bowl are assembled and sterilized as an interchangeable cartridge unit, the dangers of contamination during attachment of tubing connections are eliminated.

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*Arthur D Little Co, Cambridge, Mass

In the glycerolization phase, blood is forced onto the rotating bowl at a flow rate of approximately 50 ml per minute The bowl is rotated to give a gravitational force of 425 g The blood passes to the periphery of the bowl by centrifugal force. Separation of the blood into a heavier red cell layer at the bowl periphery and an inner lighter plasma layer occurs as the bowl fills to its capacity of 350 ml The separated plasma accumulates in the inner area of the bowl and overflows a central weir into a plastic bag After the entire unit of blood has been infused and the maximal amount of plasma collected, the plasma bag is sealed and detached from the cartridge unit for freezing. Without interruption, a large volume of 20 per cent solution of glycerol is introduced into the bowl followed by a large volume of 50 per cent glycerol As each successive glycerol solution increases in volume within the centrifuge, it traverses the packed cell residue contained within the bowl from the periphery to the central weir of the bowl and thence spills over into a discard outlet The plasma remaining in the bowl at the end of the cell separation cycle dilutes the initial portions of 20 per cent glycerol entering the bowl and a similar dilution occurs as the glycerol solution concentration is increased Glycerol equilibration between the cells and wash solution thereby progresses gradually by means of counter current dialysis Following addition of the 50 per cent glycerol solution, the centrifuge is stopped, permitting the glycerolized cells to flow into a separate plastic bag which is sealed and detached

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Blood oxygen capacity as determined by the method of Van Slyke and Neill[17] was compared with the spectrophotometric method of Hickam and Frayser,[8] using a Beckman spectrophotometer Model DU. Published density coefficients were confirmed by the standardization in a large number of normal bloods against the manometric capacity. Using our constants, 11 consecutive fresh blood samples showed a mean deviation between manometric and spectrophotometric values of −0.07 vol. per cent with a standard deviation of 0.49 vol. per cent. For 16 consecutive comparisons on samples of thawed deglycerolized ACD and heparinized blood, the mean deviation was −0.15 vol. per cent with a standard deviation of 0.40 vol. per cent. The lack of significant statistical variation between such comparisons of fresh and frozen blood oxygen capacities indicates the validity of our spectrophotometric standards and excludes the possibility of significant methemoglobin formation in the stored blood. There was no increased disparity between manometric and spectrophotometric capacity values in the older stored bloods, which ranged from 3 to 31 months' storage time.

Blood oxygen and carbon dioxide contents were determined initially by the combined manometric method of Van Slyke and Neill[17] using 1.0 ml. blood samples. Since the resulting oxyhemoglobin saturation values showed insignificant deviation from simultaneous oxyhemoglobin determinations by a spectrophotometric method, we abandoned the combined blood manometric analysis and relied in this study upon the quicker spectrophotometric method. During this later period, plasma carbon dioxide content was determined by the manometric method of Van Slyke and Neill[17] on 1.0 ml. plasma samples obtained after centrifugation under oil.

Blood hydrogen ion concentration was measured with the Beckman Model Gs pH meter with an external anaerobic electrode immersed in a 37° C. water bath. The electrode was standardized with pH 7.00 buffer solution. Microhematocrit determinations were made.[9]

Following tonometric equilibration, the gas phase within the chamber was analyzed for carbon dioxide and oxygen by duplicate determinations with the Scholander apparatus.[20] Gas tensions were computed from this analysis and the ambient barometric pressure corrected for water vapor tension.

Computation of Oxyhemoglobin Dissociation Curves.—

Oxyhemoglobin dissociation curves were constructed using the general principles of the Harvard Fatigue Laboratory as outlined by Dill in the report of Keys, Hall, and Barron.[11] The technique of computation is shown in Fig. 4. Generally between three and five observations with oxyhemoglobin saturations between 30 and 80 per cent were available to give a linear relationship between HbO_2/Hb (oxyhemoglobin/reduced hemoglobin) and corrected pO_2 when plotted on 2 by 3 cycle log-log paper. The resulting best-fit line was used to construct the conventional sigmoid dissociation curve comparing oxyhemoglobin saturation to corrected pO_2. In addition, two values were determined for each linear log-log plot to express the contour and position of the constructed linear sigmoid curve: (a) the pO_2 value where $HbO_2 = Hb$ or 50 per cent oxyhemoglobin saturation; and (b) the slope of the log-log line which represents the value "n" in the Hill-Barcroft equation expressing the general characteristics of oxyhemoglobin dissociation:

$$\frac{HbO_2}{Hb} = K\ (pO_2)^n$$

$$\text{or } \log HbO_2/Hb = \log K + n \log (pO_2)$$

The pO_2 50 per cent value represents the degree of shift of the dissociation curve to right or left of the standard position while the value "n" determines the degree of sigmoid inflection of the curve.

All pO_2 values were corrected to a standard pH_s of 7.40 by the equation:

$$\frac{\Delta \log pO_2}{\Delta pH} = K$$

Since there was no reason to suppose that the value of the constant K in this equation would be the same for degycerolized blood as for fresh blood, determinations of the constant were carried out by construction of multiple dissociation curves on aliquots of deglycerolized acid-citrate-dextrose or deglycerolized heparinized blood in which the pH was altered widely by alterations of pCO_2, or addition of lactate or sodium bicarbonate. The value of K for deglycerolized heparinized blood was found to be −0.475, standard deviation 0.060 (eight determinations). The value of K for deglycerolized acid-citrate-dextrose blood was found to be −0.2945, standard deviation 0.0117 (seven determinations: pH 6.55 → 7.44). The standard value for K of −0.480 above 7.00 pH and −0.460 below 7.00 pH was used for fresh heparinized and ACD blood corrections.[27]

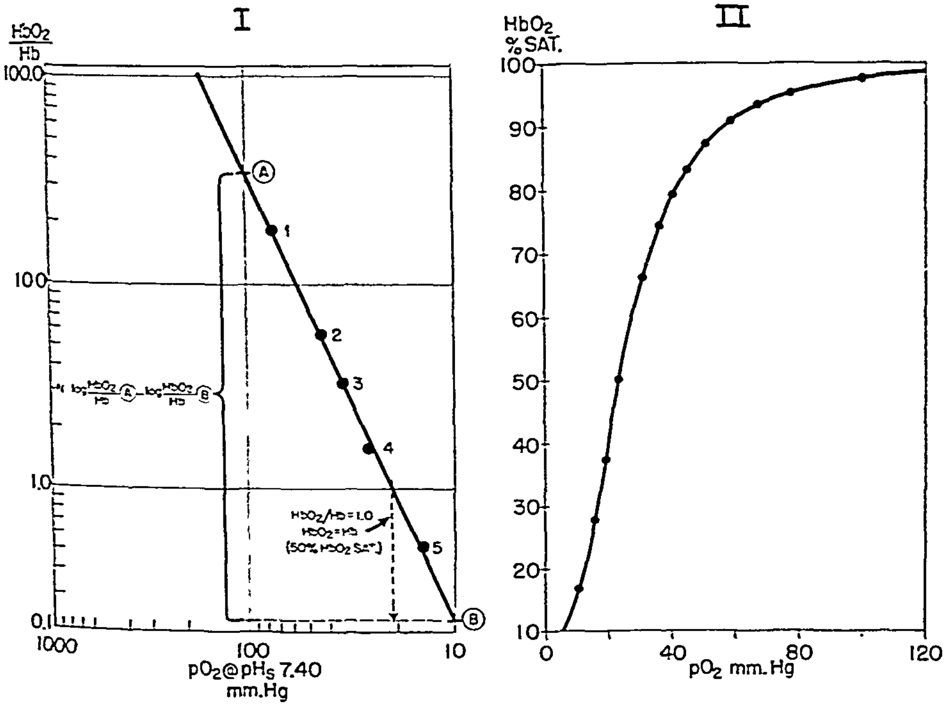


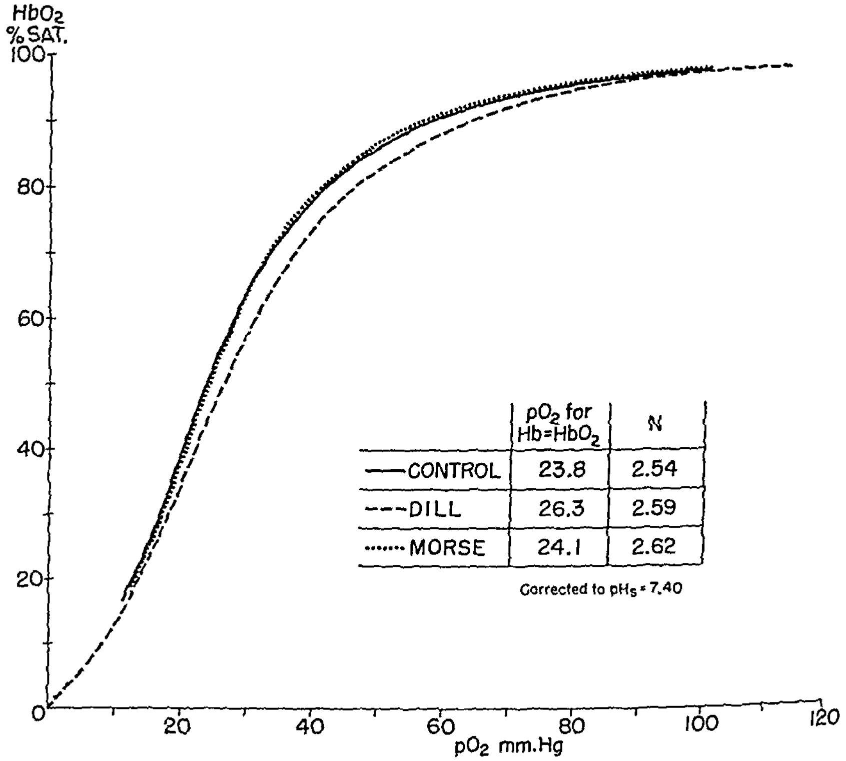
Fig 4—Method of construction of oxyhemoglobin dissociation curve Between three and five observations are made equating oxyhemoglobin saturation to pO_2 at a given pH. The saturation value is converted to the ratio: HbO_2 Hb (oxyhemoglobin per cent/reduced hemoglobin per cent) and the pO_2 value corrected to a standard pHs 7 40 equivalent. These points are then plotted on log-log paper (I) to give a straight line. Values are computed for pO_2 at which oxyhemoglobin saturation is 50 per cent and "n" representing the slope of the line. Conventional dissociation curves are constructed (II) by reading off points upon the best-fit log-log line

RESULTS

Standard Curves for Fresh Heparinized Blood From Healthy Donors and Preoperative Patients.—

To confirm the validity of our methods, six curves were constructed using fresh heparinized blood of healthy donors and patients preoperative for thoracic operation, without evidences of anemia, polycythemia, or arterial oxyhemoglobin desaturation. The conformity of the standard curve resulting from averaging these values is shown in Fig. 5. The pO_2 value for 50 per cent oxyhemoglobin saturation was 23.81 mm. Hg with a standard deviation of

3.15 mm. Hg. The value of "n" was 2.540 ± 0.13. The standard curve conforms closely to the curve of Morse[15] for adults. It is likely that the larger standard deviation for our pO_2 value results from the use of blood from an adolescent and two children in our standard curve computations. Since most of the blood donors in this series were healthy sailors in late adolescence, alterations of contour of the individual blood specimens from published adult standard curves might be expected.[3, 4, 15] Conclusions are based largely on the comparison of curves with control curves on that blood or changes in contour of the individual curves with the passage of time.



	pO_2 for $Hb=HbO_2$	N
—— CONTROL	23.8	2.54
- - - DILL	26.3	2.59
······· MORSE	24.1	2.62

Corrected to $pH_s = 7.40$

Fig. 5.—Comparison of our normal control oxyhemoglobin dissociation curve to the curves reported by Dill[3] and Morse [15]

Fresh Acid-Citrate-Dextrose Blood Preserved at 4° C.—

Contrary to the findings of Valtis and Kennedy, we found a significant shift of oxyhemoglobin dissociation to the left on the first day of storage at 4° C. In two such units, pO_2-50 per cent values were 11.0 and 17.5 mm. Hg. Valtis and Kennedy could demonstrate significant shifts only after storage of such blood at 4° C. for periods of more than 7 days.[27] We demonstrated that the shift showed progression with prolonged storage at 4° C.—a finding consistent with the observations of Valtis and Kennedy.[27]

Blood Collected in Acid-Citrate-Dextrose Solution, Glycerolized, and Frozen at –80° C. for Periods up to 31 Months.—

It was impossible to detect a significant shift of the oxyhemoglobin dissociation curve in blood immediately upon reconstitution after –80° C. storage for up to 31 months (Fig. 6). Although a slight deviation to the left from the normal curve was observed in four of five units studied, the pO_2-50 per cent value was altered less than 3.6 mm. Hg in these units, an insignificant change. Moreover, there appeared to be no consistent progression of the slight variation during successive months of –80° C. storage. It was not possible to compare dissociation curves observed before freezing with curves obtained on the same blood after storage since all units were glycerolized and frozen before the inception of this study.

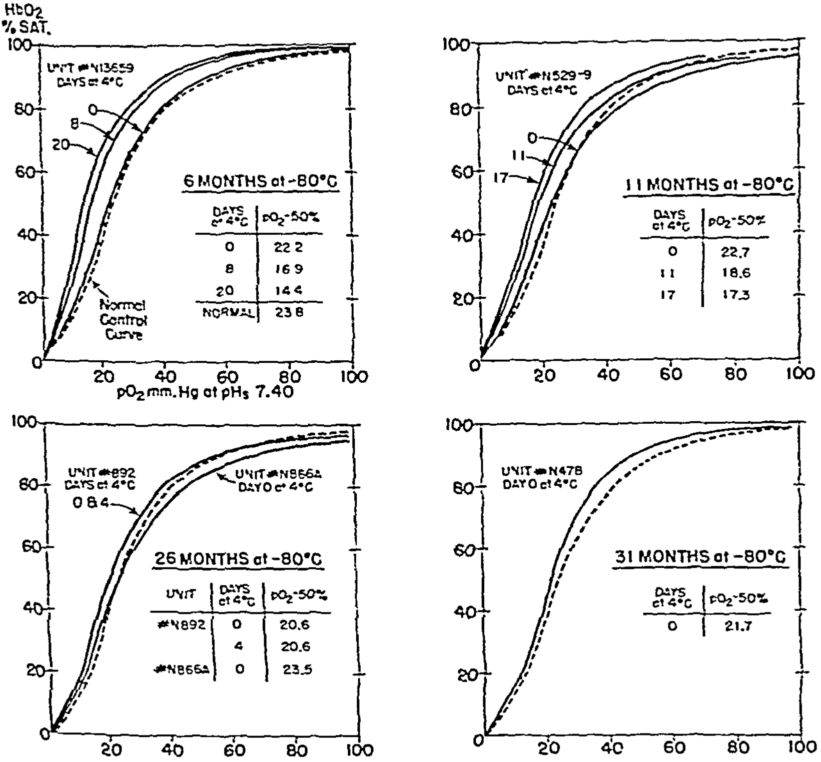


Fig. 6.—Oxyhemoglobin dissociation curves for blood collected in acid-citrate-dextrose solution and preserved for varying lengths of time at –80° C. After thawing and deglycerolization, curves were determined immediately and after several days' additional storage of the now fluid blood at 4° C. Although insignificant shifts are observed immediately upon thawing, the characteristic Valtis-Kennedy shift is observed as the blood is stored at 4° C.

The characteristic significant shift of dissociation to the left was observed, however, when these units were stored at 4° C. for periods of 8 days or over after deglycerolization and reconstitution. The magnitude of the shift at 4° C. did not appear to be greater than that observed by Valtis and Kennedy for fresh acid-citrate-dextrose blood stored at 4° C. for comparable lengths of time.[27]

Blood Collected in Heparin-Saline Solution, Glycerolized, and Frozen at –80° C. for Periods up to 7 Months.—

Table I indicates a significant shift of oxyhemoglobin dissociation to the left in curves determined immediately after reconstitution following collection in heparin, glycerolization, and freezing. Since heparinized blood is not stored at 4° C. after reconstitution but is used immediately for pump priming and transfusion, studies were not conducted to indicate progression of the shift on prolonged storage. Attention is directed to the in vivo observation that the shift was corrected in a much more rapid manner following total blood volume replacement with heparinized deglycerolized blood than with fresh acid-citrate-dextrose blood volume replacement (Fig. 7). Despite the magnitude of the early shift observed in vitro, the clinical study carried out and demonstrated in Fig. 7 suggests that correction may be so prompt that shifts comparable to those demonstrated in vitro could not be shown.

Dynamics of Oxygen and Carbon Dioxide Exchange.—

The oxyhemoglobin dissociation curve expresses the static equilibrium conditions of oxygen transport and gives no indication as to the rate at which oxygen will combine with hemoglobin in the red cell. We have used a pump-oxygenator circuit to study these dynamic changes. In one experiment, our

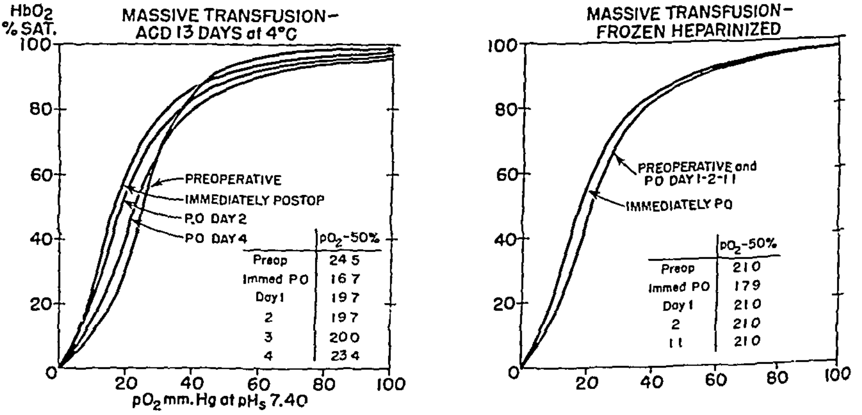


Fig 7—Studies in patients after total blood volume replacement with bank ACD blood stored by the conventional techniques at 4° C for 13 days, as compared to similar replacement with blood which had been preserved in heparin and frozen at –80° C

ACD 13 Days A 47-year-old crane operator undergoing total cardiac bypass for operative treatment of aortic stenosis received 4,500 ml of bank ACD blood late during the procedure A pronounced left-shift has not completely corrected by the fourth day of his uncomplicated convalescence (An 11-day curve was not suitable for computation because of gas analysis errors)

Frozen Heparinized· A 13-year-old girl received 4,800 ml of frozen deglycerolized heparin blood stored 5 to 12 days at –80° C during total cardiac bypass for correction of pulmonic stenosis Shift was observed immediately after operation, but curves drawn on postoperative days 1, 2, and 11 showed no significant deviation from the control curve Neither patient showed bleeding tendencies nor late difficulties

TABLE I

DAYS AT –80° C.	pO_2 FOR 50% HbO_2
2	17.2 mm. Hg
5-12	17.9
4	15.5
207	14.0
210	18.8
Mean and S.D.	16.3 ± 1.98
Normal Control Curves Mean and S.D.	23 8 ± 3.15

pump-oxygenator[25] was primed with fresh heparinized venous blood and the rate of oxygenation under standard conditions observed. In another experiment, deglycerolized heparinized blood was used in a similar manner. Since the oxyhemoglobin saturation changes were not comparable in the two experiments, direct comparisons are not possible but equation to published figures for bypasses indicates that no gross impairment of oxygenation rate is induced by the glycerolization process. In the recirculation experiment with fresh heparinized blood, we found that our disc oxygenator introduced into venous blood 2.88 ml. of oxygen per disc per minute in raising oxyhemoglobin saturation from 42 to 68 per cent. Gross and associates[6] found that their oxygenator introduced 3.0 ml. of oxygen per disc per minute at comparable saturation levels. Using deglycerolized heparinized blood (which had been stored 6 months at −80° C.) as a prime in our oxygenator, we found 2.22 ml. of oxygen per disc per minute was introduced to raise oxyhemoglobin saturation from 63 to 88 per cent. Gross and associates[6] reported an exchange of 2.0 ml. per disc per minute. Thus we conclude that no gross deficiencies in oxygen uptake dynamics exist following glycerolization of blood. Further studies are in progress to document precisely these dynamic changes as well as the conditions of carbon dioxide transport in the above experiment. The rate of change of blood pCO_2 did not significantly vary between the two types of blood.

DISCUSSION

We have confirmed the finding of Valtis and Kennedy[27] that the oxyhemoglobin dissociation curve shows a shift to the left as fresh acid-citrate-dextrose blood is preserved at 4° C. beyond 8 days. They concluded that the shift was dependent upon changes in intracellular electrolyte concentration and pH, and could be prevented by the addition of sodium chloride solution to the preserved blood to bring the final concentration of sodium chloride to 0.45 per cent.[26] The present deglycerolization technique does not result in significant shifts of the oxyhemoglobin dissociation curve during periods of storage of the citrated blood cell at −80° C. up to 31 months, despite the considerable alterations of electrolyte concentration which must occur during glycerolization and deglycerolization. However, we have demonstrated that shifts do occur early following reconstitution of heparinized deglycerolized blood. This aspect of the problem is under investigation since it is just this blood which should possess a normal oxyhemoglobin dissociation pattern at all times in view of its use in pump-oxygenator perfusions. Although the shift appears to be rapidly correctable once the blood is infused in the body, elimination of the effect would be desirable. At the present time, our washing solutions in the deglycerolization phase are designed to bring heparinized blood to a pH of 7.10, comparable to that of acid-citrate-dextrose blood. This pH has been shown to give maximal survival of red cells when blood is stored at 4° C. The use of large volumes of heparinized deglycerolized blood at this pH in extracorporeal perfusions has not resulted in serious body acid-base disturbances but we would prefer to have our wash solutions adjusted in the future to allow for a more physiologic pH early during a perfusion. There is no necessity for keeping heparinized deglycerolized blood at a pH of 7.1 since it is not stored for long periods of time after reconstitution and hence should not necessarily meet the requirement of acidity indicated for reconstituted acid-citrate-dextrose blood. This latter blood after reconstitution is kept for days at 4° before conventional transfusion therapy while reconstituted heparinized blood is withdrawn from the freezer and used promptly on reconstitution. As a consequence, our present investigations are aimed at (a) adjusting final washing solutions in the deglycerolization phase to bring the thawed deglycerolized blood to a pH of 7.4, and (b) to increase the sodium chloride content of the washing solutions just sufficiently to eliminate the Valtis-Kennedy shift observed for frozen heparinized blood. It is hoped that the latter maneuver will eliminate the shift without producing serious derangements of plasma electrolyte concentrations in the final reconstituted blood package. The ability to perform these various adjustments easily and without loss of blood sterility is a great advantage of the glycerolization freezing process.

SUMMARY

1. Blood treated with glycerol and stored for prolonged periods of time at -80° C. may be used as a suitable medium for pump priming and transfusion in cardiovascular surgery. The glycerolization process requires the separation of cells from plasma and addition of glycerol to the cell fraction in a modified Cohn fractionator.

2. Blood collected in acid-citrate-dextrose solution and preserved at -80° C. for up to 31 months demonstrates no deviation of oxyhemoglobin saturation curve comparable to that which has been demonstrated for fresh acid-citrate-dextrose blood stored at 4° C. beyond 7 days by conventional blood banking techniques.

3. Blood collected in heparin-saline solution, glycerolized, and frozen shows a significant shift of the oxyhemoglobin dissociation curve to the left when reconstituted after 4 to 210 days' storage. On infusion of such blood into a patient as a total blood volume replacement, the shift is corrected in less than 1 day. Similar shifts induced by total blood volume replacement with bank ACD blood stored over 13 days at 4° were not corrected completely at the end of 4 days.

4. The rate of exchange of oxygen and carbon dioxide in a pump-oxygenator is the same for deglycerolized heparinized blood as for fresh heparinized blood.

5. Studies are in progress to adjust the technique of cell washing so that the addition of sodium chloride to the reconstituted heparinized blood will eliminate the oxyhemoglobin dissociation shift.

Lt. (jg) John W. Zemp collaborated with us and performed many of the analyses reported. We are also indebted to Capt. Lewis L. Haynes, Chief of Surgery, U. S. Naval

Hospital, Commander Mary V. Sproul, and Dr. James L. Tullis and associates (of the Protein Foundation, Inc.) for encouragement and advice. They are not responsible for any errors noted by the reader. This work would not have been possible without the assistance of J. A. Cavins, Lt. (MC) USNR, and the prolonged labor by our technicians in the Preservation Laboratory, B. C. Sutherland HM-2, USN, M. Bethea, HMC USN, and our pump technicians, Mr. Ralph Sommers and Mr. Joel Johns.

REFERENCES

1. Brown, I. W., Jr., and Hardin, H. F.: Recovery and In Vivo Survival of Human Red Cells: Studies of Red Cells After Storage up to 6¼ Months at Subzero Temperatures, A. M. A. Arch. Surg. 66: 267-282, 1953.
2. Cohn, E. J.: Blood Collection and Preservation in American Association of Blood Banks. Proceedings. Fourth Annual Meeting, Minneapolis, Minn., Oct. 22-24, 1951.
3. Dill, D. B.: Handbook of Respiratory Data in Aviation. Washington, D. C., 1944, National Research Council.
4. Drabkin, D. L.: Aspects of the Oxygenation and Oxidative Function, in Haemoglobin: A Symposium Based on a Conference Held at Cambridge in June, 1948, in Memory of Sir Joseph Barcroft, edited by F. J. W. Roughton and J. C. Kendrew, New York, 1949, Interscience Publishers, Inc., pp. 36 45.
5. Gordy, E., and Drabkin, D. L.: A Simplified Spectrophotometric Technique Applicable to Standard Equipment for Determinations of O_2 Saturation of Blood, Proc. Soc. Am. J. Med. Sc. 221: 231-232, 1951.
6. Gross, R. E., Sauvage, L. R., Pontius, R. G., and Watkins, E., Jr.: Experimental and Clinical Studies of a Siphon-Filling Disc Oxygenator System for Complete Cardiopulmonary Bypass, Ann. Surg. 151: 285 302, 1960.
7. Haynes, L. L., Tullis, J. L., Pyle, H. M., Sproul, M. T., Wallach, S., and Turville, W. C.: Clinical Experiences With the Use of Glycerolized Frozen Blood, J. A. M. A. 173: 1657-1663, 1960.
8. Hickam, J. B., and Frayser, R.: Spectrophotometric Determination of Blood Oxygen, J. Biol. Chem. 180: 457-465, 1949.
9. Jones, A. R.: Device for Rapidly Deriving Hematocrit of Blood Centrifuged in Ungraduated Tubes, New England J. Med. 254: 172-174, 1956.
10. Ketchel, M. M., Tullis, J. L., Tinch, R. J., Driscoll, S. G., and Surgenor, D. M.: Use of Biomechanical Equipment for the Long-Term Preservation of Erythrocytes, J. A. M. A. 168: 404-408, 1958.
11. Keys, A., Hall, F. G., and Barron, E. S. G.: Position of the Oxygen Dissociation Curve of Human Blood at High Altitude, Am. J. Physiol. 115: 292-307, 1936.
12. Lovelock, J. E.: Mechanism of Protective Action of Glycerol Against Haemolysis by Freezing and Thawing, Biochim. et biophys. acta 11: 28-36, 1953.
13. Merryman, H. T.: Ice Crystal Formation in Frozen Tissues. Lecture and Review Series 53-3 Naval Medical Research Institute, 1955, March 27, pp. 1-44.
14. Mollison, P. L., Sloviter, H. A., and Chaplin, H., Jr.: Survival of Transfused Red Cells Previously Stored for Long Periods in Frozen State, Lancet 2: 501-505, 1952.
15. Morse, M., Cassels, D. E., and Holder, M.: Position of Oxygen Dissociation Curve of Blood in Normal Children and Adults, J. Clin. Invest. 29: 1091-1097, 1950.
16. Nahas, G. G.: Spectrophotometric Determination of Hemoglobin and Oxyhemoglobin in Whole Hemolyzed Blood, Science 113: 723-725, 1951.
17. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry. Volume II: Methods, Baltimore, 1932, Williams & Wilkins Co.
18. O'Brien, T. G., Haynes, L. L., Hering, A. C., Tullis, J. L., and Watkins, E., Jr.: The Use of Glycerolized Frozen Blood in Vascular Surgery and Extracorporeal Circulation, Surgery (in press).
19. O'Brien, T. G., and Watkins, E., Jr.: Prolonged Heparin Activity in Stored Blood Processed by the Glycerolization Freezing Method. (To be published.)
20. Scholander, P. F.: Analyzer for Accurate Estimation of Respiratory Gases in One-Half Cubic Centimeter Samples, J. Biol. Chem. 167: 235-250, 1947.
21. Sloviter, H. A.: In Vivo Survival of Rabbit's Red Cells Recovered After Freezing, Lancet 1: 1350-1351, 1951.
22. Sproul, M. T., and Sloane, M. H.: The Present Status of Research on Red Blood Cell Preservation and Plasma Sterilization in the United States. P. H. Andresen, papers in dedication of his sixtieth birthday, Copenhagen, 1957, Munksgaard, pp. 170 188.
23. Stainsby, W. N., Fales, J. T., and Lilienthal, J. L., Jr.: Rapid Spectrophotometric Method for Determining Oxygen Content of Dog's Blood, J. Appl. Physiol. 7: 577-579, 1955.

24. Tullis, J. L., Ketchel, M. M., Pyle, H. M., Pennell, R. B., Gibson, J. G., II, Tinch, R. J., and Driscoll, S. G.: Studies on the In Vivo Survival of Glycerolized and Frozen Human Red Blood Cells, J. A. M. A. 168: 399-404, 1958.
25. Tullis, J. L., and others: New Principle of Closed System Centrifugation, Science 124: 792-797, 1956.
26. Valtis, D. J., and Kennedy, A. C.: Causes and Prevention of Defective Function of Stored Red Blood Cells After Transfusion, Glasgow M. J. 34: 521-543, 1953.
27. Valtis, D. J., and Kennedy, A. C.: Defective Gas-Transport Function of Stored Red Blood-Cells, Lancet 1: 119-125, 1954.
28. Watkins, E., Jr., Hering, A. C., and Adams, H. D.: Design and Use of a Pump Oxygenator, S. Clin. North America 40: 609-632, 1960.

(For Discussion, see page 631)

THE RELATIONSHIP OF THE SYMPATHO-ADRENAL SYSTEM TO POTASSIUM FLUX AND CARDIAC IRRITABILITY INDUCED BY ALTERATIONS IN BLOOD pH

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Richard C. Lillehei, M.D., and Fletcher A. Miller, M.D. (by invitation),
Minneapolis, Minn.

PREVIOUS experiments in this laboratory have indicated that rapid reversal of the arterial pH to normal after prolonged inhalation of carbon dioxide has a far more deleterious effect upon cardiac function in the dog than the antecedent acidosis.[1, 2] Arrhythmias thus invoked frequently culminate in ventricular fibrillation, a sequence of events which may have a counterpart in clinical cases of unexplained cardiac arrest.[1, 4] Data will be presented herein demonstrating that during this critical period a rapid loss of myocardial potassium and a significant diminution of plasma levels of circulating catecholamines occur.

During hypercapnia there is a gradual rise in the levels of serum potassium, phosphorus, and glucose with a concomitant drop in the level of ultrafiltrable calcium. In the immediate post-hypercapnic period, instead of the normal relationship of these ions being restored, there is a further divergence, the ratio of calcium to potassium dropping to one third of the control.[3] This critical period has a temporal relationship to the onset of arrhythmias and fibrillation, which may, however, be prevented by measures designed to maintain a normal ratio of ion concentrations.[5]

The knowledge that levels of catecholamine in plasma are elevated during respiratory acidosis, along with our previous demonstration that epinephrine administration prevented post-hypercapnic ventricular fibrillation,[6] suggested to us that the rapid changes in ion concentration when the blood pH is suddenly advanced to normal might be associated with a drop in circulating catecholamine levels. This stimulated further investigation concerning the relationship of the sympatho-adrenal system to the fluctuations in ion concentration that occur with changes in pH and/or carbon dioxide tension.

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METHOD

The following groups of experiments were carried out on healthy mongrel dogs.

Group I.—In 7 dogs, simultaneous sampling of potassium levels in arterial and coronary sinus blood were performed during respiratory acidosis and in the critical post-hypercapnic period, plus analysis of plasma epinephrine and norepinephrine during the same period.

Group II.—In 14 dogs, measurements of potassium were carried out as in Group I, except that these animals were treated with either epinephrine or norepinephrine in the immediate post-hypercapnic period.

Group III.—In this experiment, arterial and coronary sinus potassium levels were measured in 13 normocapnic dogs following rapid intravenous administration of epinephrine or norepinephrine in a dosage sufficient to produce arrhythmias (8 micrograms per kilogram of body weight).

Group IV.—In this series of 8 dogs, the experiments were similar to Group III, save that the liver was excluded from the circulation by clamping the hepatic artery and portal vein prior to administration of the catecholamines.

Group V.—This consisted of the measurement of arterial potassium levels during the inhalation of 30 per cent carbon dioxide in oxygen in a series of 8 adrenalectomized dogs.

The standard experimental technique of inducing ventricular fibrillation following respiratory acidosis, as described previously, was employed.[2] In addition, in each animal a cardiac catheter was inserted into the coronary sinus via the jugular vein under fluoroscopic control. The position of the catheter was subsequently checked at autopsy. Simultaneous samples of arterial and coronary sinus blood were obtained at appropriate intervals for potassium analysis. Electrocardiographic and blood pressure tracings were recorded intermittently.

Plasma catecholamines were measured by the technique of Weil-Malherbe and Bone.[7]

TABLE I. PLASMA CATECHOLAMINE LEVELS DURING INHALATION OF CARBON DIOXIDE AND IN THE IMMEDIATE POST-HYPERCAPNIC PERIOD

		ACIDOSIS			POST-ACIDOSIS	
	CONTROL	15 MIN. CO_2(30%)	2 HOURS CO_2(30%)	4 HOURS CO_2(40%)	3 MIN.	8 MIN.
Epinephrine (microgram/L.) (mean)	0.29	1.51	2.06	5.44	1.35	3.20
Standard error	±0.1	±0.53	±0.38	±1.06	±0.45	±0.98
Norepinephrine (microgram/L.) (mean)	2.09	4.41	5.08	9.40	5.80	5.68
Standard error	±0.2	±0.62	±0.55	±1.01	±0.95	±0.97
Blood pH (mean)				6.73	7.39	
Standard error				±0.01	±0.03	

RESULTS

Group I.—The results in this group are summarized in Fig. 1. It can be seen that, as the dog inhales carbon dioxide, the potassium level gradually rises in both the arterial and coronary sinus blood, but there is no *significant* difference between these two sites. After 4 hours on carbon dioxide the pH has dropped to 6.7 and the potassium levels in the arterial and coronary sinus samples are almost identical. In the immediate post-hypercapnic period there is a definite rapid rise of the potassium in both systems; however, the coronary sinus samples were consistently higher by an average of 1.5 mEq. per liter.

The epinephrine and norepinephrine titers during this same period are summarized in Table I. A gradual rise in both of these substances occurs throughout the period of acidosis, particularly when the animal inhales 40 per cent carbon dioxide. This is in complete agreement with data previously reported by Nahas.[8] In the post-hypercapnic period, at the identical time when the potassium divergence described in Fig. 1 is maximal, these levels dropped precipitously.

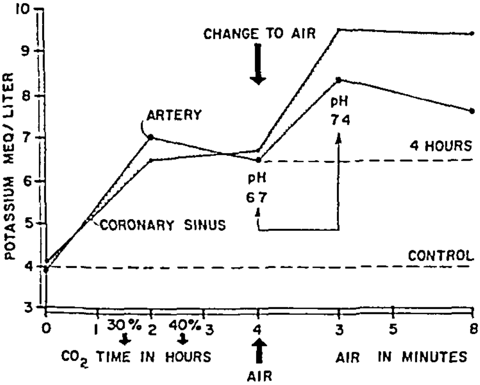

Fig. 1.—This graph illustrates changes occurring in the levels of potassium in arterial and coronary sinus blood during respiratory acidosis and in the immediate post-hypercapnic period in a series of 7 dogs. The negative arteriovenous difference in the post-hypercapnic period occurred consistently in all of the experiments. The difference ranged from –0.7 to –2.7 mEq./L. at 3 min. and from –0.7 to –3.0 mEq./L. at 8 min.

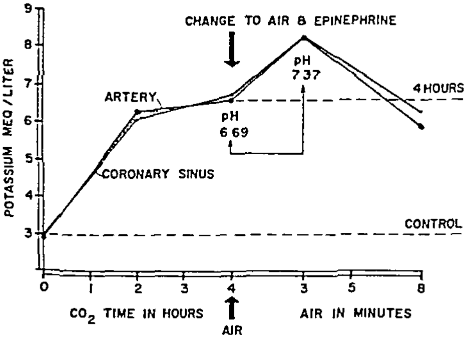

Fig. 2.—This graph illustrates the average effect on potassium levels in a series of 7 experiments wher [illegible] tered in the post-hypercapnic period. The virtual elimination of the [illegible] difference that occurs in control dogs during this period was a consis [illegible] experiments. The difference ranged from –0.5 to +3.5 mEq./L. at 3 min. and from –1.3 to +0.5 mEq./L. at 8 min. Similar results were obtained in a series of 7 dogs when norepinephrine was administered during this period.

Group II.—When epinephrine or norepinephrine is administered in the post-hypercapnic period continuously intravenously, at a rate sufficient to maintain (adequately) the systemic blood pressure, the serum potassium rises but divergence of the potassium levels does not occur; this is demonstrated in Fig. 2. The arrhythmias seen in this period are more typical of an epinephrine effect and generally rapidly revert to normal.

Group III.—Fig. 3 illustrates the changes that occur in the levels of arterial and coronary sinus potassium when either epinephrine or norepinephrine in a dose of 8 micrograms per kilogram is rapidly administered to normocapnic dogs. There is a biphasic effect with arterial potassium rising more rapidly than that of the coronary sinus to reach peak levels at 1 to 1½ minutes and then dropping gradually below the coronary sinus levels. It is of interest that, although the peak in arterial potassium occurs at 60 to 90 seconds, the greatest arteriovenous difference occurs earlier and is associated with severe arrhythmias.

Group IV.—Exclusion of the liver from the circulation by the method described does not prevent the arrhythmias following infusion of epinephrine or norepinephrine despite the fact that there is no rise in potassium levels or any major arteriovenous difference, as illustrated in Figs. 4 and 5.

Group V.—Adrenalectomy did not prevent the arterial potassium rise in dogs breathing 30 per cent carbon dioxide for 1 hour. The dogs were intolerant of higher carbon dioxide levels or more prolonged periods of exposure.

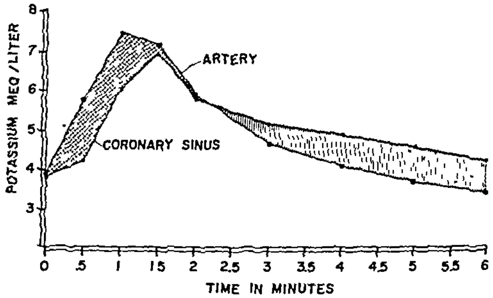

Fig. 3.—This graph illustrates the average changes that occur in the levels of potassium in arterial and coronary sinus blood when epinephrine was administered to a series of 13 normocapnic dogs in a dosage of 8 micrograms per kilogram of body weight. This biphasic effect was a consistent finding and could [illegible] lministration of norepinephrine. The arteriovenous difference was usually [illegible] and ranged from +0.7 to +3.5 mEq./L. for epinephrine and from +0.5 tc [illegible] epinephrine.

DISCUSSION

Dogs inhaling high concentrations of carbon dioxide exhibit a gradual, although significant, sustained rise in blood levels of potassium, epinephrine, and norepinephrine. Tenney[9] has suggested that the serum potassium elevation is the result of release from the liver following sympatho-adrenal stimulation. However, since we were able to demonstrate an elevation of the serum potassium in the adrenalectomized animals, it must be presumed that this hepatic response can be triggered by stimuli other than the catecholamine release from the adrenal glands.

Fenn[10] postulates that, with the inhalation of high concentrations of carbon dioxide, large quantities of potassium are released from the liver, sufficient to raise serum levels over and above a shift of potassium into the tissues, which he believes occurs under these conditions. The absence of any significant arteriovenous divergence during the inhalation of carbon dioxide, as shown in Figs. 1 and 2, should not necessarily be construed as indicating lack of myocardial potassium uptake, for Brown[11] has recorded markedly increased rates of coronary flow during this period; such an increase in flow could diminish the potassium differential below the range of analytical accuracy.

The post-hypercapnic period is characterized by a negative arteriovenous difference in potassium levels. This represents a rapid directional flux of potassium from the myocardium immediately prior to the development of ventricular fibrillation. In addition, a precipitous fall in levels of catecholamine occurs during this critical phase.

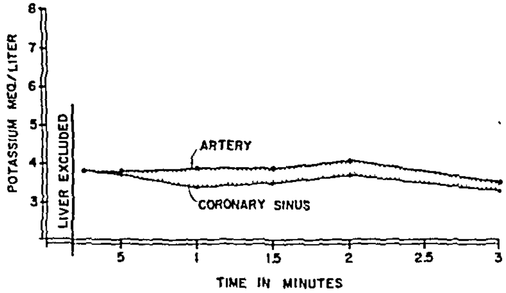

Fig. 4.—This graph illustrates the effects of epinephrine on arterial and coronary sinus potassium after exclusion of the liver from the circulation. Dosage 8 micrograms per kilogram. Average of eight experiments. Arterial potassium does not rise and the arteriovenous difference remains within the range of analytical error and ranges from +0.2 to +0.8 mEq./L.

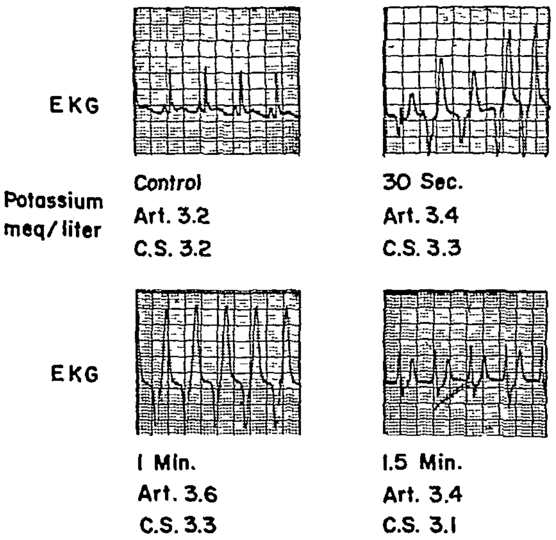

Fig. 5.—This illustration shows the effect upon the electrocardiogram of epinephrine (16 micrograms per kilogram of body weight) after exclusion of the liver from the circulation. Arterial and coronary sinus potassium levels are shown.

Since epinephrine or norepinephrine administration during the critical post-hypercapnic period protects against ventricular fibrillation, it is of added significance that these substances, as shown in Fig. 2, will also prevent the rapid loss of myocardial potassium that normally occurs in the posthypercapnic period. In fact, in some dogs, administration of these drugs effected a reversal to a positive difference. In normocapnic dogs, epinephrine and norepinephrine regularly caused a positive arteriovenous difference as shown in Fig. 3, indicating an uptake of potassium by the heart. We were not able to demonstrate such uptake of potassium after exclusion of the liver from the circulation.

In conclusion we are advancing the hypothesis that the development of ventricular fibrillation in the post-hypercapnic phase may be due to a very rapid loss of potassium from the myocardium incident to a drop in plasma catecholamine levels, and that epinephrine or norepinephrine protects the heart under such conditions by preventing this rapid potassium flux. Our data indicate that the rapidity of loss of myocardial potassium is more important in initiating the fibrillation than the mere rise of serum potassium in the circulating blood.

SUMMARY

1. During respiratory acidosis there is a rise in the potassium levels in both arterial and coronary sinus blood. There is no significant difference in these levels while acidosis is maintained but, in the immediate post-hypercapnic period, there is a further rapid rise in these levels, that of the coronary sinus being much higher which indicates loss of myocardial potassium. This period of significant arteriovenous difference has a temporal relationship to severe cardiac arrhythmias.

2. Plasma levels of epinephrine and norepinephrine are elevated during respiratory acidosis. The post-hypercapnic period is associated with a precipitous drop in the previously high levels. This too has a temporal relationship to the arrhythmias occurring at this time.

3. The administration of epinephrine or norepinephrine to normocapnic dogs has a biphasic effect on myocardial potassium flux.

4. Exclusion of the liver from the circulation prevents the rise in levels of potassium that result from the administration of epinephrine or norepinephrine, but does not necessarily prevent arrhythmias. Significant arteriovenous differences in potassium levels were not detected by the method employed.

5. The administration of epinephrine or norepinephrine in the post-hypercapnic period eliminates the negative arteriovenous difference in levels of potassium and prevents the occurrence of ventricular fibrillation.

REFERENCES

1. Miller, F. A., Brown, E. B., Buckley, J. J., Van Bergen, F. H., and Varco, R. L.: Respiratory Acidosis: Its Relationship to Cardiac Function and Other Physiologic Mechanisms, Surgery 32: 171-183, 1952.
2. Brown, E. B., Jr., and Miller, F. A.: Ventricular Fibrillation Following a Rapid Fall in Alveolar CO_2 Concentration, Am. J. Physiol. 169: 56-60, 1952.
3. Brown, E. B., Jr., and Prasad, A. S.: Plasma Ultrafiltrable Calcium Concentration in Posthypercapnic Ventricular Fibrillation, Am. J. Physiol. 190: 462-466, 1957.
4. Greene, N. M.: Fatal Cardiovascular and Respiratory Failure Associated With Tracheotomy, New England J. Med. 261: 846, 1959.
5. Goott, B., and Miller, F. A.: Prevention of Posthypercapnic Ventricular Fibrillation in Dogs, J. Thoracic Surg. 38: 630-638, 1959.

6 Miller, F. A Ph D. Thesis Studies in Respiratory Acidosis The Graduate School, University of Minnesota, December, 1955, pp 143 145

7 Weil Malherbe, H , and Bone, A D · Adrenergic Amines in Human Blood, Lancet 1: 974 977, 1953

8 Nahas, G G , and Ligou, J. C : Influence du pH et des catecholamines sur la consommation en oxygene du chien Des comptes rendus des seances de l'Academie des Sciences t 248, p 2132 2134, April 6, 1959.

9 Tenney, S M · Sympatho adrenal Stimulation by Carbon Dioxide and the Inhibitory Effect of Carbonic Acid on Epinephrine Response, Am J Physiol 187: 341 346, 1956

10 Fenn, O , and Tomoaki, A. Effects of Carbon Dioxide Inhalation on Potassium Liberation From the Liver, Am. J Physiol 185: 567 576, 1956.

11 Brown, E B Jr , and Mowlem, A · Potassium Loss From the Heart During the Immediate Posthypercapnic Period, Am J Physiol (To be published).

DISCUSSION

(PAPERS BY ROE [PAGE 561], MUNOZ [PAGE 568], MCCAUGHAN [PAGE 574], MEREDITH [PAGE 582], MOULDER [PAGE 588], MCLAUGHLIN [PAGE 602], O'BRIEN [PAGE 611], GOOTT [PAGE 625], AND THEIR ASSOCIATES)

DR FREDERICK S. CROSS, Cleveland Ohio—In the process of developing a subcoronary aortic valve prosthesis Drs Gerein, Richard Jones and I have gone off on the tangent of developing a single leaflet type prosthesis Certainly, there are clinical instances when this will be entirely satisfactory, if not preferable to replacing the entire aortic valve.

Our work has been divided into the proper design of the leaflet, and techniques of insertion The leaflet that we have been using is constructed over a cast of the sinus of Valsalva area, utilizing particularly the noncoronary cusp It consists of a backing of polyurethane, to which is sutured, at the present time, pericardium either as a single or double layer The leaflet is rather easily inserted through a longitudinal incision A single suture is placed to anchor the apex with an instrument remarkably similar to the one described by Dr Roe A layer of continuous sutures is then placed across the top edge of the backing

[Slide] From this slide showing the valve in systole it can be seen that the prosthetic pericardial leaflet is remarkably similar in the way it "floats" open to the normal valves In reviewing the movies of valve function, it is difficult to distinguish the prosthetic cusp from the normal ones if one does not see the suture line shown here

[Slide] This slide shows the leaflet to be perfectly competent during diastole The competency of the valve after placement of the prosthetic monocusp has been checked with aortic pressure tracings

[Slide] Unfortunately, the pericardium does not hold up well, and there is an early deposit of fibrin at the point of its contact with the other valve leaflets which in a period of about 60 hours ends up looking like this

Now as I said, although the materials that we have are not entirely satisfactory, I think the design of the leaflet is good, and the future of this work lies in the utilization of other natural tissues, such as segments of vein, rather than pericardium, and in the development of complete plastic leaflets and entire aortic valves utilizing this basic design

DR CHARLES A. HUFNAGEL, Washington D C—Dr Potts once said that if a man once has an idea that he thinks is really new, that he will love it like a son forever, even though it turns out to be a moron (laughter) I hope this is not necessarily true in that we have always continued our interest in aortic valve replacement, and our interest has been in doing this in the normal aortic position We have accomplished aortic valve replacement both in terms of single cusp replacement, multiple cusp replacement, and single unit valve replacement

[Slide] With the advent of new approaches to the aortic diseases we have developed the method of cardioplegia produced by local cold alone We have now almost 100 patients with periods of cardiac arrest ranging from 30 minutes to an hour and 40 minutes with no instance of difficulty—major difficulty—in resuscitation. Most of these patients have had some form of aortic valve surgery, and approximately 50 have had replacement of either one or more cusps.

The mortality rate in this group has been approximately 28 per cent over-all, and in the last 20 patients it has been less than half of this figure. None of these fatalities has been due to failure of the heart to resume a satisfactory beat.

This shows one of the types of cusp which is currently in use and which seems to be highly adaptable.

[Slide] This is a valve composed of a Dacron cusp which is impregnated with silicone rubber. The self-sealing feature of this cusp necessitates only a few sutures at the base, and healing occurs into this edge of the self-seal which is cloth alone. Tissue does not grow into this but into the leaflet itself, and this preserves the elasticity of the leaflet.

[Slide] It has been our impression experimentally that when tissue grows into a cloth leaflet, it stiffens, and we have had to reoperate upon 1 patient because of this stiffening. This is the cloth, impregnated with rubber.

[Slide] This shows another view of the same thing.

[Slide] This is a more sophisticated version of this for the noncoronary cusp with a stape in the cusp edges. This makes fixation extremely rapid. We have usually placed the cusps in the coronary cusp by using sutures as Dr. Roe described in his beautiful presentation of this total valve replacement.

It seemed to us that the annulus of the aorta is still a scalloped curve, and we strongly believe that the base of the artificial valve or cusp must also follow this curve. This area is the true annulus which is tremendously tough, and which holds sutures well. When one tries to follow a constant single plan, one must either enter myocardial fiber or aorta, and the tissue adjacent to the annulus of the aorta is soft.

[Slide] This shows a further adaptation on account of the sealing. The three cusps are a single unit, and this also utilizes the single principle of what we have termed a self-seal, which minimizes the use of a housing. This is a highly functional total valve replacement with which we are highly gratified.

DR. ROBERT W. OLWINE, Boston, Mass.—While considering possible methods for extraction of calcium deposits from diseased heart valves, Dr. Watkins and I thought of applying the principle of the Stryker cast cutter in shattering rigid plaster without disturbance of soft dressings and tissue. We found that a 26,500 cycle ultrasonic sound probe applied directly to autopsy specimens of calcified valves efficiently shattered and extracted the calcified concretions.

We thought, however, it was necessary to determine exactly what damage might occur to adjacent soft tissue. The ultrasound probe was applied directly to the septal leaflet of a number of normal dog tricuspid valves. Immediately after application of the ultrasound probe, petechiae were seen on the valve cusp. This specimen shows a valve that was treated approximately 35 days prior to sacrifice, demonstrating an organized hematoma on the valve cusp. The cusp is becoming sclerotic.

This slide shows a lesion that is approximately 86 days old, demonstrating considerable sclerosis and thickening of the valve cusp.

This is another specimen at 77 days [slide] and shows essentially the same changes.

The essential histologic pattern is that of a rather bizarre, loose, fibrous structure somewhat myxomatous in nature within the valve cusp substance.

It is also interesting to note that there is no apparent damage occurring to the conduction system or to the aortic valve directly opposite the point of ultrasound application.

We would like to emphasize that there are certain dangers associated with some of the techniques that are being used for extraction of calcium concretions from valves We might have, in ultrasonic sound a useful tool for the experimental production of valvular lesions permitting subsequent study of the hemodynamic changes occurring in hearts which have had a chronic lesion closely resembling that of rheumatic heart disease

DR DON R MILLER, Kansas City, Kans —In Dr Allbritten's absence I would like to bring attention to the blood phase which, in addition to the gas permeability of the membranes, appears to be important in the oxygen uptake by blood in membrane oxygenators

[Slide] We have been working in the laboratory using a membrane device of basic design similar to the Clowes oxygenator, but which utilizes simplified supported Silastic membrane bags in which are incorporated features to induce mixing within blood films and to control thickness of blood films One of the bags is shown in this slide

Basic studies by Thomas Marx of the Midwest Research Institute, designer of this oxygenator, indicate there is laminar flow in conventional models of membrane oxygenators and a static layer of blood [slide], which is depicted rather simply here, adheres to the surface of the membrane and acts as a barrier to the uptake of oxygen by the blood not in immediate contact with the membrane

[Slide] The advancing interface between saturated and unsaturated blood has been photographed in this static blood film experiment in which blood in a diffusion cell separated from oxygen by this membrane was observed through a Lucite plate This static layer increases the distance through which oxygen must diffuse before reaching the unsaturated blood The introduction of internal flow obstructions to produce turbulence within the blood film has resulted in greater oxygen uptake, even with thicker blood films than those used in the laminar flow experiments

Other changes which theoretically should increase oxygen uptake in the blood phase, but which are more difficult to accomplish in a membrane oxygenator, are greater velocity to decrease the thickness of the static layer and thinner blood films to decrease the length of the oxygen diffusion path

DR PAUL F WARE, Worcester, Mass —I would like to present very briefly, if I may, one other method of getting at this problem, particularly for those of us who perhaps are only occasional members of perfusion groups and must use every parameter we possibly can for safe monitoring

[Slide] We have been using in the laboratory and also clinically a type of reflection oximeter developed by Dr M Polanyi of the American Optical Company and tested by Hehir in the chemistry laboratories of the St Vincent Hospital

Now, it's very difficult to use a spectrophotometric method, because we do destroy samples The method is lengthy, and it doesn't give us the information we need in the course of perfusion Originally, Zijlstra did produce a reflection oximeter, and this was further developed by Rodrigo They used, however, only one wave length, and this type has had very little application clinically

In our type of oximeter two wave lengths are utilized It is an absolute oximeter You can use it with either dog blood or human blood and you do get a practically instantaneous recording Other virtues are that it is independent of hemoglobin content, oxygen saturation, or temperature

[Slide] Just briefly, this is a simple tungsten lamp at this point, cuvette, and blood sample There is an angle of 135 degrees here, and the density of the blood is reflected back There are interference filters here which make the blood density concentrate in a very narrow wave length back on the photo cell

[Slide] Utilizing these two wave lengths, we then can prove that the light, diffusely reflected by an unhemolyzed sample, is correlated with the oxygen saturation You choose wave lengths, such as has been done here, to give a maximum difference between the extinction coefficients of oxyhemoglobin and reduced hemoglobin.

Utilizing this present instrument with these wave lengths, you don't have to worry about the intensity of the incident light. You don't have to think about the geometry of your arrangement, and the difference between individual blood samples doesn't enter into your calibration.

This slide simply shows that the ratio of light reflected by a nonhemolyzed blood sample is a linear function of the oxygen saturation.

[Slide] This is simply to show how small an arrangement in space is actually necessary. This is a standard pump-oxygenator, Olson type. One can run a small line off the arterial line—also off the venous line—run it through the oximeter; one simply pinches the tubing for a few seconds and takes a reading. This gives you an instantaneous recording of what the actual venous or arterial oxygen saturation is. We have found this very convenient for use clinically.

DR. WILLIAM H. LEE, JR., Charleston, S. C.—The departments of surgery and pharmacology at the Medical College of South Carolina also have been interested in these observations of the rebound arrhythmias which occur following periods of acidosis. I just wanted to bring up the fact that other stimuli besides hypercapnia can set off the same reaction.

[Slide] For example, in this slide, which shows the epinephrine and norepinephrine levels which occur following azygos flow—this is used to produce a situation with a hypoxic or ischemic acidosis, and during the 10-minute phase of reduced (azygos) flow, one sees a fairly marked depression in cardiac contractile force, despite a marked increase in the concentration of norepinephrine and epinephrine.

In this instance, following the azygos flow period, there is a rather marked rebound. In this particular group of experiments, we found that there is a direct relationship between the contractile force of the heart and the concentration of these two substances when the pH is sufficiently high to allow the heart to respond to this stimulation—that is, in the range of 7.3 or above.

[Slide] This is a similar experiment which shows the azygos flow preparation, again with marked rebound in the middle tracing (contractile force). Sometimes the catecholamine levels may be one hundred times the control levels.

[Slide] The same situation occurs here—again a rebound—except that it is produced by an unusually low flow rate during cardiac bypass (20 c.c./Kg./min.) rather than by azygos flow.

[Slide] Concerning the infusion of epinephrine, this slide demonstrates the inability of the heart to respond to arterenol stimulation during acidosis, whether it be hypercapnic or metabolic, produced by ischemic flow rates. The arterial pH during azygos flow is noted to be high. After the venae cavae are released, there is a marked rebound in cardiac contractile force and a fall in arterial pH with an associated decrease in responsiveness to arterenol stimulation. As the cardiac output and tissue perfusion returns to normal, the pH progressively rises and the response to arterenol injection returns to control values. During this latter phase, an increased irritability of the heart has been observed.

This slide shows the effect of rapid arterenol infusion. The infusion of arterenol, in itself, may produce a metabolic acidosis, as one sees the pH values begin at 7.6 and drop down to 7.26, after 105 minutes of the perfusion.

BRONCHOSCOPY AND BACTERIEMIA

Sheldon Oscar Burman, M.D. (by invitation), Pittsburgh, Pa.*
*With the technical assistance of Miss Mollie L. Hill, M.T. (A.S.C.P.)***

IN THE ROUTINE diagnosis and treatment of pulmonary disease, bronchoscopy is an essential and commonplace adjunct. Facility in the technique of bronchoscopy is one of the earliest skills acquired by the thoracic surgical resident and its use is normally attended by little immediate mortality or obvious morbidity. Nevertheless, the post-bronchoscopic course of many patients is frequently marked by the appearance of a mild fever of 1° to 3° F. which occurs about 4 hours following the procedure, lasting perhaps 24 hours, and often passing unnoticed. The etiology of this fever has heretofore been a subject of speculation and has been variously ascribed to one or more of these mechanisms: (1) retention of secretions from depression of the cough reflex and inhibition of ciliary motility due to preoperative sedation and to the anesthesia employed; (2) the implantation of pyogen-laden secretions into previously uninfected parts of the lung; (3) auto-tuberculinization, or the host's response to the foreign protein presumably liberated from traumatized organisms; and (4) autoreaction of the host to blood liberated from bronchoscopic trauma to the endobronchial mucosa.

In a tuberculosis hospital most bronchoscopies are performed just before operation, after prolonged antituberculous chemotherapy, to verify the absence of active endobronchial disease. Nearly all of these patients have clean, dry, tracheobronchial trees, with stable, nonexudative disease, and the bronchoscopy is usually easy, swift, and relatively atraumatic. Indeed, the incidence of an intrabronchial pathologic condition is so low that the need for bronchoscopy has been seriously questioned.[16] Thus, it seemed to us that the accepted and time-honored explanations for the post-bronchoscopy fevers were not pertinent to most of our patients. Because fever accompaning endoscopy by other routes, particularly urethral, is known to be related to transitory bacteriemia, we undertook to determine whether the fevers associated with bronchoscopy might have their origin in the dissemination of blood-borne bacteria.

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Read at the Fortieth Annual Meeting of The American Association for Thoracic Surgery at Miami Beach, Fla., May 11-13, 1960.

*Teaching Fellow in Thoracic Surgery.

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PROCEDURE

A total of 52 patients undergoing bronchoscopy, 50 with tuberculosis and 2 with bronchogenic carcinoma, were studied as follows: careful records of the state of their disease and previous antibiotic therapy were kept. The daily temperatures for the week preceding, and on the morning of, bronchoscopy were recorded. A rectal temperature was taken upon the patient's return to the ward, 2 hours later, then every 6 hours for 2 days. During bronchoscopy the presence or absence of endobronchial inflammation, purulent secretions, and traumatic bleeding was noted. In all cases, 5 per cent topical cocaine anesthesia was used. The sputa or gastric washings of all patients except 1 were repeatedly negative on culture for tubercle bacilli before bronchoscopy but acid-fast bacilli were present in smears of 2. One patient yielded organisms both on smear and culture. The disease was radiographically stable in all cases.

After preparing the skin with 70 per cent alcohol and tincture of iodine, 15 c.c. of venous blood was drawn for culture just before, 10 minutes after, 2 hours after, and 4 hours after bronchoscopy. If a fever of 1° F. or more occurred at any time within the next 2 days, blood was drawn again for culture. Duplicate blood samples of 5 c.c. each were inoculated into sterile, 8 oz., screw-top bottles containing a trypticase-agar slant and 50 c.c. of trypticase-soy broth. Cultures were grown under aerobic and anaerobic conditions and inspected twice daily for 21 days. For cultures of the tubercle bacillus, blood was inoculated into agar, Dubos, and oleic acid media (two parts blood and eight parts medium) and inspected twice daily for 10 days. Where growth was noted, transplantation was done to thioglycolate broth, methylene-blue agar, inulin agar, mannitol broth, and 7.5 per cent sodium chloride brain-heart infusion broth. If, at the end of 21 days, no growth was noted the trypticase-soy broth was centrifuged, a smear made, and stained with Gram's stain. If organisms were seen on the smear, the sediment was subcultured. At the end of 10 days, all the blood from each patient's combined samples for tubercle bacilli was pooled, digested with sodium hydroxide and hydrochloric acid, centrifuged, and smears were prepared and stained for acid-fast bacilli with carbolfuchsin stain.

Of the 52 patients studied, none was found by bronchoscopy to have purulent secretions and none was febrile before or at the time of bronchoscopy. Mild abrasion of the bronchial mucosa with a little bleeding occurred with 2 patients.

Although it is recognized that nonhemolytic staphylococci can produce serious disease, positive blood cultures containing these organisms were excluded from this series because they are common contaminants. To be acceptable, all staphylococci were required to exhibit hemolysis and to grow in a 7.5 per cent sodium chloride brain-heart infusion medium.

RESULTS

Twenty-four (46 per cent) patients had 1° to 3° F. of fever beginning 4 hours after bronchoscopy. No significant fever was detected earlier than 4 hours after the procedure. Six patients had fever lasting more than 6 hours and in 3 of these the fever persisted for 24 hours. Of the 24 patients with fever, 8 (33.3 per cent) produced positive blood cultures. No positive blood cultures were found in samples collected before bronchoscopy and no positive cultures during or after bronchoscopy were obtained from nonfebrile patients. The following bacteria were isolated from the blood: 2 patients had gamma streptococci, 3 patients had *Streptococcus viridans,* 2 patients had hemolytic *Staphylococcus albus,* and 1 patient had both *Streptococcus viridans* and *Escherichia coli.* All organisms grew under aerobic conditions with the exception of one of the gamma streptococci which was an anaerobe. All cultures yielded moderate to heavy growth. One positive blood culture was obtained during bronchoscopy, five were obtained 2 hours following bronchoscopy, and two were obtained 4 hours after the procedure. Although 6 patients had fevers lasting more than 6 hours after bronchoscopy, no positive cultures were grown from later specimens. No cultures positive for tuberculosis were found in any of the samples. It is conceivable that with larger and more frequent sampling a higher percentage of positive cultures might have been obtained.

DISCUSSION

It has been well established that bacteriemia may be induced by dental or urological manipulation.[3, 10, 15] Okell and Elliott[11] observed a transient bacteriemia (preponderantly the alpha streptococcus) following dental extraction in 72 per cent of patients with oral infections and in 32 per cent of those without obvious sepsis. Burket and Burn[2] demonstrated the dental origin of the bacteriemia by implanting a nonpathogen *(Serratia marcescens)* around the teeth and then recovering it from the blood stream following intra-oral manipulation. The same phenomenon has been observed by Elliott[5] after tonsillectomy. The incidence of bacteriemia following transurethral prostatic resection, as reported by Merritt,[8] and by Creevy and Feeney[3] ranges from 12 to 45 per cent. Cystostomy, cystoscopy, and urethral catheterization have all been responsible for inducing not only transient bacteriemia but also subacute bacterial endocarditis.[6] The causative organisms in these cases is usually the enterococcus (a variety of streptococcus), the Friedlander's bacillus (*Klebsiella pneumoniae*), *Escherichia coli,* or *Pseudomonas aeruginosa.* Bacteriemia and endocarditis have been known to follow hemorrhoidectomy, and McCoy and Mason[9] have reported it in conjunction with carcinoma of the sigmoid colon. Unterman, Milberg, and Kranis[14] have suggested an association between sigmoidoscopic examination and subsequent bacteriemia.

The mouth and pharynx notoriously abound with bacterial flora but as one advances in an aboral direction, the bacterial population diminishes sharply until by the time the bronchi and lungs are reached, as Pecora and Yegian[12] have shown, cultures are usually sterile, even in chronic lower respiratory tract disease. Expectorations and bronchial aspirates frequently represent merely the flora of the mouth and pharynx. The most common organisms in these areas are the staphylococci, streptococci, Neisseria, and coliforms, and these organisms are precisely the cause of 95 per cent of all cases of bacterial endocarditis.[6] During normal activity, such as chewing, tooth brushing, and probably defecating, bacteria apparently enter the blood stream, having, in fact, been cultured from the blood of normal individuals,[13] with little or no apparent harm. However, bacterial endocarditis seldom occurs in a previously normal heart[6] although it can be induced experimentally in subjects with normal hearts by repeated intravenous injection of nonhemolytic streptococci.[4, 7] In patients with acquired or congenital valvular disease, on the other hand, bacteriemia is a serious threat.

The majority of patients undergoing bronchoscopy appear to suffer few immediate ill effects from it. But the onset of bacterial endocarditis is insidious and may escape clinical detection, particularly in the presence of other concomitant disease. Despite the availability of curative antibiotics, bacterial endocarditis is lethal in about 25 per cent of all cases and the threat is greatest in the older age groups. This present study suggests that prophylactic antibiotic treatment and attention to oral hygiene is indicated prior to bronchoscopy in all patients with rheumatic or congenital heart disease for these are most susceptible to bacterial endocarditis. For patients with valvular heart disease, the American Heart Association now recommends the administration of 600,000 units of aqueous penicillin and 600,000 units of procaine penicillin 30 minutes before dental extraction and it would appear reasonable to extend this practice to those patients undergoing bronchoscopy. Also, because of the increasing incidence of organisms not sensitive to penicillin, the additional use of a wide-spectrum antibiotic is suggested.

CONCLUSION AND SUMMARY

1. Approximately 50 per cent of a series of patients undergoing bronchoscopy responded with a fever of 1° to 3° F. beginning about 4 hours after the procedure.

2. Of these, 33.3 per cent were shown to have suffered a transitory bacteriemia.

3. The organisms isolated were the alpha and gamma streptococci, hemolytic *Staphylococcus albus,* and *Escherichia coli.*

4. The danger of bacteriemia in patients with congenital or rheumatic cardiovalvular disease is stressed.

5. A program of oral hygiene and antibiotic prophylaxis is urged for patients with congenital or acquired cardiovalvular disease in whom bronchoscopy is contemplated.

REFERENCES

1. Beeson, P. B., Brannon, E. S., and Warren, J. V.: Observations on Sites of Removal of Bacteria From Blood From Patients With Bacterial Endocarditis, J. Exper. Med. 81: 9, 1945.
2. Burket, L. W., and Burn, C. G.: Bacteriemias Following Dental Extraction. Demonstration of Source of Bacteria by Means of a Non-pathogen, Serratia Marcescens, J. D. Res. 16: 521, 1937.

3. Creevy, C. D., and Feeney, M. J.: Infection Following Transurethral Resection of Prostate Gland, Bull. Univ. Minnesota Hosp. 20: 319, 1949.
4. Dick, G. F., and Schwartz, W. B.: Experimental Endocarditis of Dogs, Arch. Path. 42: 159, 1946.
5. Elliott, S. D.: Bacteriemia Following Tonsillectomy, Lancet 2: 589, 1939.
6. Friedberg, C. K.: Diseases of the Heart, Philadelphia and London, 1956, W. B. Saunders Company, chap. 34, p. 861.
7. Libman, E., and Celler, H. L.: Etiology of Subacute Infective Endocarditis, Am. J. M. Sc. 140: 516, 1910.
8. Merritt, W. A.: Bacterial Endocarditis as Complication of Transurethral Prostatic Resection, J. Urol. 65: 100, 1951.
9. McCoy, W. C., and Mason, J. M., III: Enterococcal Endocarditis Associated With Carcinoma of the Sigmoid; Report of a Case, J. M. A. Alabama 21: 162, 1951.
10. Middleton, W. S., and Burke, M.: Streptococcus Viridans Endocarditis; Clinico-Pathological Analysis of Experience in Wisconsin General Hospital, Am. J. M. Sc. 198: 301, 1939.
11. Okell, C. C., and Elliott, S. D.: Bacteriemia and Oral Sepsis With Special Reference to Etiology of Subacute Bacterial Endocarditis, Lancet 2: 869, 1935.
12. Pecora, D. B., and Yegian, D.: Bacteriology of the Lower Respiratory Tract in Health and Chronic Diseases, New England J. Med. 258: 74, 1958.
13. Schatten, W. E., Desprez, J. D., and Holden, W. D.: Bacteriologic Study of Portal Vein Blood in Man, A. M. A. Arch. Surg. 71: 404, 1955.
14. Unterman, D., Milberg, M. B., and Kranis, M.: Evaluation of Blood Cultures After Sigmoidoscopy, New England J. Med. 257: 773, 1957.
15. Weiss, H.: Relation of Portals of Entry to Subacute Bacterial Endocarditis, Arch. Int. Med. 54: 710, 1934.
16. Wilson, N. J.: Tr. Eighteenth Conference on Chemotherapy of Tuberculosis, Remarks following discussion, p. 89. VA Department of Medicine and Surgery, Central Office, Washington, D. C.

(For Discussion, see page 699)

ALTERED HEMODYNAMICS IN THE PULMONARY CIRCULATION FOLLOWING REAERATION OF AN ATELECTATIC LUNG

Edwin T. Long, M.D. (by invitation), William E. Adams, M.D.; John R. Benfield, M.D. (by invitation), Takemaru Mikouchi, M.D. (by invitation), Arthur F. Reimann, M.D. (by invitation), and Salvatore Nigro, M.D. (by invitation), Chicago, Ill.

A CURIOUS DISCREPANCY has been reported by four independent observers concerning patients who have had long-term chronic atelectasis of one lung followed by surgical intervention and reaeration of the lung. These patients have had generally satisfactory degrees of return of function but bronchospirometry studies have regularly shown a discrepancy between ventilation and oxygen uptake in the reaerated lung. Its contribution to total oxygen uptake has been significantly lower than its contribution to total ventilation.[7, 12, 16, 19] This phenomenon has not been explained in the general consensus that reaerated atelectatic lungs regain their function after reinflation.

The subject of atelectasis and the question of its reversibility have been areas of continuing interest in this laboratory.[1, 3, 11] Benfield and his associates[3] demonstrated that in dogs an average of 14 per cent of the cardiac output was shunted through chronically atelectatic left lungs. However, the shunt was eliminated by occluding the pulmonary artery to these lungs or by surgical intervention and reaeration of the lungs. Doubt was cast on the complete reversibility of chronic atelectasis by the observation that animals with a reaerated left lung did not survive contralateral pneumonectomy. The animals died with a boggy, edematous condition in the remaining reaerated lung and they exhibited a large dilated right ventricle with a passively congested liver. Another animal with a reaerated lung following chronic atelectasis was studied during balloon cardiac-catheter occlusion of the pulmonary artery to the unaffected lung. This animal developed significant pulmonary hypertension during the period of occlusion and the peripheral arterial oxygen saturation dropped markedly.

The significance of these observations was not immediately apparent. The following experiments were designed to determine the physiologic value of a reaerated chronic atelectatic lung.

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Read at the Fortieth Annual Meeting of The American Association for Thoracic Surgery at Miami Beach, Fla., May 11-13, 1960.

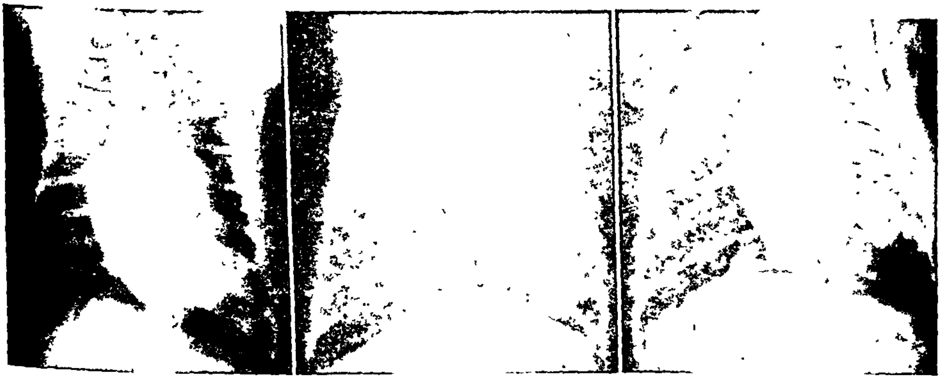
METHOD

Two groups of mongrel dogs, weighing 10 to 20 kilograms each, were used.

Group I.—12 animals. Two animals were controls.

Ten animals were subjected to chronic atelectasis of the entire left lung produced by closing the left main bronchus. This was accomplished either by bronchoscopic cautery, using 35 per cent silver nitrate solution resulting in subsequent bronchial stenosis or by surgical division of the bronchus and suture closure of the cut bronchus ends at thoracotomy.[1, 17] The atelectasis was confirmed by physical examination, bronchoscopy, fluoroscopy, and radiographic means.

After 4 to 67 weeks of atelectasis, left thoracotomy was performed with resection of the closed portions of the bronchus with end-to-end anastomosis of the opened bronchial ends, using continuous 4-0 black silk atraumatic suture material with everting technique. Before starting the bronchial anastomosis the distal bronchial tree was aspirated to remove the accumulated mucus that always filled but did not distend the bronchial system. After completing the anastomosis, the small, airless, liver-like lung was reinflated with positive pressures up to 35 mm. Hg. The lungs reaerated at lower pressures but did not resume more than 50 to 75 per cent of estimated normal size even with the highest pressures used. The reaerated lungs were pale. Postoperative chest roentgenograms were made (Fig. 1).



A. B C.

Fig. 1.—*A*, Normal chest film.

B, Chest film which shows complete atelectasis of the left lung. The aerated lung visible above the diaphragm on the left is an enlarged accessory lobe of the right lung herniated across the midline.

C, Chest film made 4 days after left thoracotomy, bronchoplasty, and reaeration of the atelectatic lung.

Four to 120 weeks after reaeration, an evaluation of the pulmonary functions was made. Each animal was anesthetized with a continuous intravenous drip of 0.2 per cent Surital after premedication with atropine sulfate, 0.0004 Gm., and morphine sulfate, 0.015 to 0.075 Gm. Bronchospirometric ventilation studies were made using a specially constructed tracheal divider and two Benedict-Roth recording spirometers with balloon-boxes filled with either air or 26 per cent oxygen. To ensure proper position of the tracheal divider, insertion was made under fluoroscopic control using a "carina finder" as a guide (Fig. 2). After inflating the balloon on the tracheal divider to 35 mm. Hg, a test was made by hyperinflating each lung separately under fluoroscopic control. This served the dual purposes of indicating any leaks and of showing the degree to which the lungs could be expanded (Fig. 3).

Arterial blood samples were collected from a femoral artery. Mixed venous blood samples were obtained from the pulmonary artery via cardiac catheter. Blood-oxygen content was obtained by the method of Van Slyke and Neill. Cardiac output was calculated using the direct Fick method.

Group II.—24 animals. Four animals were controls.

Twenty animals were subjected to chronic atelectasis of the entire left lung for 3 to 67 weeks. This was followed by surgical reaeration of the atelectatic lungs. The methods used were the same as described for Group I.

Three to 137 weeks after reaeration, the pulmonary artery pressure was studied under intravenous 0.2 per cent Surital anesthesia using a cardiac catheter, Statham P23Db strain gauge, and Grass recorder. After obtaining a satisfactory base line pulmonary artery pressure, the right pulmonary artery was temporarily occluded either by balloon cardiac-catheter obstruction (closed chest) or by cross-clamping the artery at thoracotomy (open chest). Completeness of the balloon cardiac-catheter obstruction of the right pulmonary artery was determined by cessation of oxygen uptake on that side of a bronchospirometric tracheal divider.

With the right pulmonary artery blocked, the entire cardiac output was diverted through the left reaerated lung, hemodynamically duplicating acute right pneumonectomy.

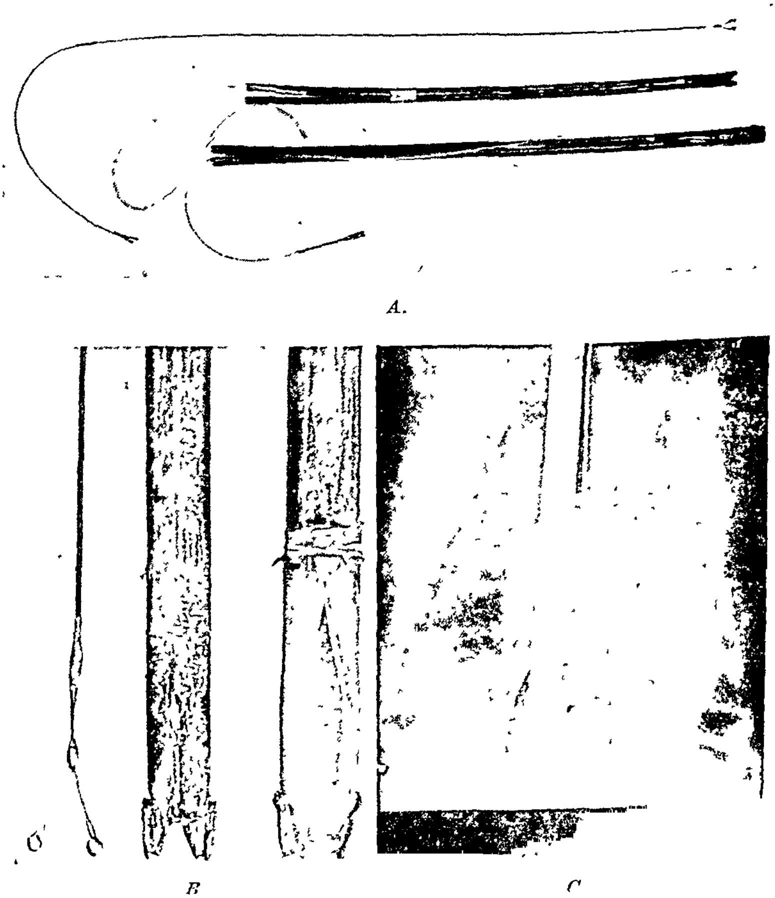


Fig. 2.—*A*, "Carina finder" and two tracheal dividers, one without balloon to show details. *B*, Close-up view of the same instruments. The "carina finder" is made of piano wire and solder. The tracheal dividers are made of two large copper tubes and one small copper tube soldered together. The two large tubes have been compressed in a vise to make the cross-section of each an oval. Thus, the cross-section of the assembled divider approaches a circle.

C, Chest film which shows the "carina finder" astride the carina (bronchoscopically placed) and the tracheal divider in the *wrong* position completely within the right main bronchus. When placement is correct, the crotch of the tracheal divider is coincident with the crotch of the "carina finder" fluoroscopically (see Fig 3—*A*, *B*, *C*).

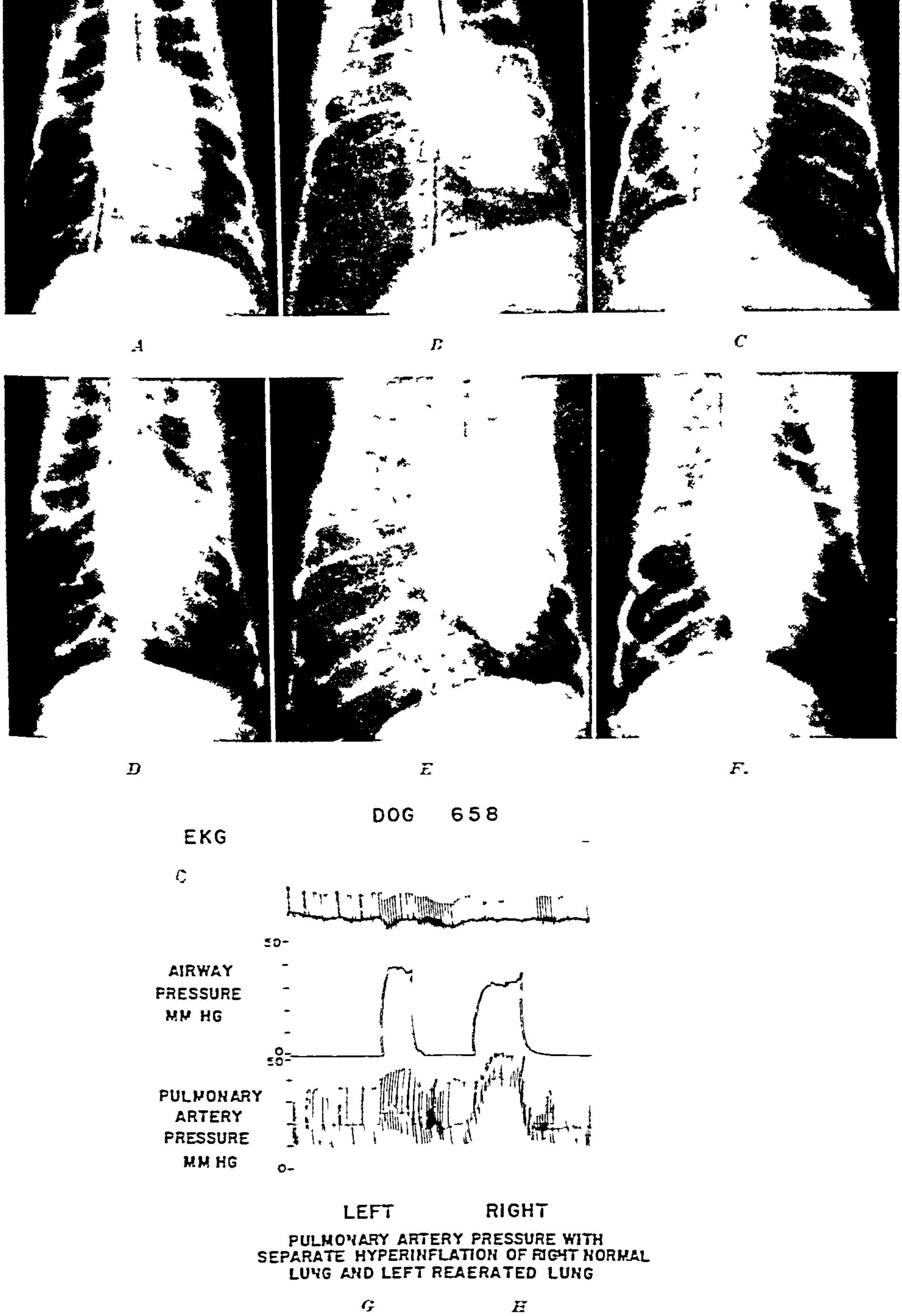

A
B
C
D
E
F
DOG 658
EKG
C
50
AIRWAY PRESSURE MM HG
0
50
PULMONARY ARTERY PRESSURE MM HG
0
LEFT
RIGHT
PULMONARY ARTERY PRESSURE WITH SEPARATE HYPERINFLATION OF RIGHT NORMAL LUNG AND LEFT REAERATED LUNG
G
H

Fig. 3.—*A*, Normal control animal with tracheal divider in place.

B, Same animal with right lung hyperinflated.

C, Same animal with left lung hyperinflated.

D, Experimental animal with reaerated left lung after 21 weeks of chronic atelectasis. Tracheal divider in place.

E, Same animal with right lung hyperinflated. Compare with *B* above.

F, Same animal with left lung hyperinflated. Compare with *C* above.

G, Same animal's pulmonary artery pressure response during hyperinflation of the left lung as shown in *F* above.

H, Same animal's pulmonary artery pressure response during hyperinflation of the right lung as shown in *F* above.

TABLE I. BRONCHOSPIROMETRY AND CARDIAC OUTPUT ST

	1†	2	3	4	5	6	7	8
	DOG NO.	WEEKS OF ATELECTASIS	WEEKS OF REAERATION	O_2 MIXTURE	ART. O_2 (VOL. %)	ART. O_2 SAT. (%)	VEN. O_2 (VOL. %)	VEN. O_2 SAT. (%)
A*	L18	0	0	26%	20.90	84	16.13	64
B	L17	0	0	Air	18.06	90	14.03	70
C	Average of 2 control animals							
1†	P28	4	40	Air	19.84	89	15.64	70
2	P3N	4	4	26%	18.33	90	15.87	78
3	P923	7	50	26%	19.85	92	14.70	67
4	P164	18	48	26%	24.38	96	19.39	76
5	P658	20	21	26%	19.25	91	15.43	74
6	P189	20	120	26%	19.79	94	15.56	74
7	P271	25	40	Air	21.30	81	17.16	65
8	P831	42	36	Air	16.10	70	12.61	55
9	P425	52	20	26%	20.02	98	16.17	79
10	P62	67	4	26%	21.44	97	16.85	76
11	Average of 10 experimental animals							

*Lines A and B contain data from control animals.
†Lines 1 through 10 contain data from the experimental animals.

Histopathologic Study.—Biopsies of the lungs of 5 of the above animals were obtained. The left lungs were biopsied in the atelectatic and reaerated states. The right lungs were biopsied only after reaeration of the left lungs. The biopsies were processed routinely by the Department of Pathology, The University of Chicago, and reviewed by Dr. Eleanor Humphreys, Professor Emeritus of Pathology.

RESULTS

There were advantages to both methods of atelectasis production. In the bronchus cautery method, atelectasis was produced without the injury of a thoracotomy and at the reaeration operation no adhesions were found. However, it was variable in its convenience and predictability if cautery was limited to a short, easily resectable length of bronchus. The method of surgical division of the bronchus was quick and easy but involved pleural trespass with a variable degree of adhesions found at the reaeration operation. There was no noticeable difference between the two methods in ease or degree of reaeration of the atelectatic lungs.

Group I.—Fluoroscopic observation of hyperinflation of the reaerated left lungs regularly demonstrated a markedly reduced compliance. All the reaerated lungs were considerably limited in their ability to expand. The loss of compliance was seemingly more significant in the upper portions of the lungs; the lower lobes expanded fairly well (Fig. 3).

The response of pulmonary artery pressure to the hyperinflation maneuver was quite revealing. When the right lung was hyperinflated, the pulmonary artery pressure elevation was proportional to the inflating pressure.[18] But when the reaerated left lung was hyperinflated, the pulmonary artery pressure was affected only slightly (Fig. 3).

The bronchospirometric pulmonary function data and the Fick cardiac output data are presented in Table I.

WITH REAERATED LEFT LUNGS AFTER CHRONIC ATELECTASIS

	11	12	13	14	15	16	17	18
G)	V O_2 RIGHT (% OF TOTAL)	V O_2 LEFT LUNG (C.C./M.)	V O_2 LEFT (% OF TOTAL)	CARDIAC OUTPUT L./M. (FICK)	VENT. RIGHT LUNG (L./M.)	VENT. RIGHT LUNG (% OF TOTAL)	VENT. LEFT LUNG (L./M.)	VENT. LEFT LUNG (% OF TOTAL)
	57	25.0	43	1.23	1.20	60	.80	40
	62	17.5	38	1.13	1.13	57	.85	43
	59.5		40.5			58.5		41.5
	79	15.0	21	1.76	3.9	71	1.6	29
	82	10.0	18	2.28	1.5	76	.5	24
	77	20.6	23	1.73	1.78	76	.55	24
	100	0	0	1.50	3.3	83	.70	17
	86	10.0	14	1.83	1.92	65	1.00	35
	100	0	0	1.41	1.93	91	.18	9
	65	17.0	35	1.18	1.03	62	.63	38
	89	12.0	11	3.20	2.5	82	.55	18
	100	0	0	1.35	2.2	76	.7	24
	83	12.5	17	1.67	2.1	72	.8	28
	86.1		13.9			75.4		24.6

The use of 26 per cent oxygen in the spirometer-balloon box system seemed to help in keeping arterial oxygen saturation above 90 per cent during the bronchospirometry study. Of the 4 animals with arterial oxygen saturation over 93 per cent, 3 had no oxygen uptake in the left lung and the fourth had an oxygen uptake of 17 per cent of the total (Table I, columns 6 and 12, lines 4, 6, 9, 10).

The contribution to both ventilation and oxygen uptake of the left lung of the control animals was approximately 40 per cent of total. The contribution to ventilation of the reinflated left lung of the 10 experimental animals averaged 24.6 per cent of total and to oxygen uptake was only 13.9 per cent of total. There was an absolute increase in right lung oxygen uptake and an absolute decrease in left lung oxygen uptake compared to controls (Table I, columns 13 and 18, lines C and 11; Table I, columns 10 and 12).

Group II.—The pulmonary artery pressure data are presented in Tables II and III and Fig. 4.

Table II: The base line mean pressures of the control animals averaged 13.0 mm. Hg and the mean pressures with right pulmonary artery occlusion averaged 20.0 mm. Hg. The base line pulmonary artery mean pressures of the 20 experimental animals averaged 16.2 mm. Hg and, with right pulmonary artery occlusion, they averaged 36.0 mm. Hg. This occlusion value is over 200 per cent of base line mean pressures for the experimental animals and almost 300 per cent of the base line mean pressures for the control animals. The experimental animals did not tolerate the occlusion of the right pulmonary artery without distress. The distress was relieved by removing the occlusion.

Table III: There was apparently little difference in the qualitative results whether the temporary occlusion of the right pulmonary artery was produced by balloon cardiac-catheter occlusion (closed chest) or by cross-clamping at thoracotomy (open chest). Base line pulmonary artery pressures were higher in the open chest experiments.

TABLE II. PULMONARY ARTERY PRESSURE STUDIES OF ANIMALS WITH REAERATED LEFT LUNGS AFTER CHRONIC ATELECTASIS

	DOG NO.	WEEKS OF ATELECTASIS	WEEKS ELAPSED TO PRESSURE TEST	METHOD OF PA OCCLUSION	PAP RT. & LT. PA OPEN (MM./Hg.)		PAP LT. PA OCCLUDED (MM./Hg.)		PAP RT. PA OCCLUDED (MM./Hg)	
A*	C1	0	0	Balloon, closed chest	18/6	10	25/4	11	33/9	17
B	C2	0	0	Balloon, closed chest	22/15	17	28/22	24	32/27	29
C	C3	0	0	Thoracotomy, open chest	23/10	15	—	—	22/8	13
D	C4	0	0	Thoracotomy, open chest	21/4	10	—	—	33/15	21
Average of 4 control animals						13.0		17.5		20.0
1†	P1N	3	35	Balloon, closed chest	25/5	12	—	—	38/18	26
2	P3N	4	8	Balloon, closed chest	25/7	12	27/10	13	40/12	22
3	P5N	4	13	Thoracotomy, open chest	25/17	19	—	—	50/26	34
4	P2N	4	15	Thoracotomy, open chest	24/10	15	—	—	55/27	35
5	P28	4	15	Balloon, closed chest	25/10	15	35/10	18	45/20	28
6	P923	7	55	Balloon, closed chest	28/7	15	33/10	18	35/15	24
7	P961	9	137	Balloon, closed chest	25/7	12	—	—	45/10	28
8	P10N	11	8	Balloon, closed chest	35/8	20	40/11	21	67/28	42
9	P164	18	48	Balloon, closed chest	22/5	12	33/8	18	75/25	40
10	P149	20	8	Balloon, closed chest	25/5	13	35/10	18	50/15	27
11	P189	20	120	Balloon, closed chest	22/10	14	27/12	16	40/17	25
12	P271	25	76	Thoracotomy, open chest	32/12	17	—	—	45/17	27
13	P124	26	121	Thoracotomy, open chest	27/17	20	—	—	50/25	33
14	P8N	35	6	Thoracotomy, open chest	46/22	27	—	—	100/50	72
15	P7N	36	4	Thoracotomy, open chest	33/12	20	—	—	82/40	58
16	P9N	36	4	Thoracotomy, open chest	45/20	30	—	—	75/32	48
17	P822	38	3½	Balloon, closed chest	23/2	9	—	—	83/18	49
18	P425	52	23	Balloon, closed chest	22/7	12	24/12	16	50/25	38
19	P299	61	34	Thoracotomy, open chest	23/10	15	—	—	60/15	33
20	P62	67	4	Balloon, closed chest	35/9	16	—	—	75/10	31
Average of 20 experimental animals						16.2		17.2		36.0

*Lines A through D contain the data from control animals.
†Lines 1 through 20 contain the data from the experimental animals.

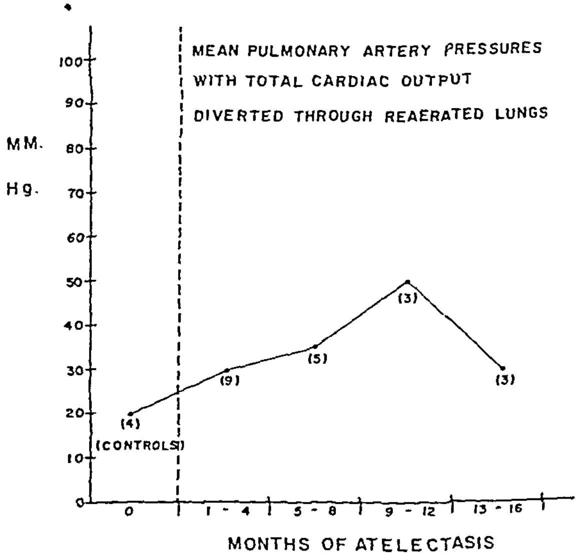


Fig. 4.—Mean pulmonary artery pressures with total cardiac output diverted through reaerated left lungs after chronic atelectasis.

TABLE III. PULMONARY ARTERY PRESSURE STUDIES OF ANIMALS WITH REAERATED LEFT LUNGS AFTER CHRONIC ATELECTASIS*

	OBSTRUCTION OF PULMONARY ARTERY BY BALLOON CARDIAC CATHETER (CLOSED CHEST)			OBSTRUCTION OF PULMONARY ARTERY BY CROSS-CLAMPING AT THORACOTOMY (OPEN CHEST)			
	BASE LINE PAP	OCCLUSION OF LEFT PA	OCCLUSION OF RIGHT PA	BASE LINE PAP	OCCLUSION OF LEFT PA	OCCLUSION OF RIGHT PA	
A	18/6 10	25/4 11	33/9 17	23/10 15	—	22/8 13	C
B	22/15 17	28/22 24	32/27 29	21/4 10	—	33/15 21	D
Average of controls	13.5	17.5	23.0	12.5		17.0	
1	25/5 12	—	28/18 26	25/17 19	—	50/26 34	3
2	25/7 12	27/10 13	40/12 22	24/10 15	—	55/27 35	4
5	25/10 15	35/10 18	45/20 28	32/12 17	—	45/17 27	12
6	28/7 15	33/10 18	35/15 24	27/17 20	—	50/25 33	13
7	25/7 12	—	45/10 28	46/22 27	—	100/50 72	14
8	35/8 20	40/11 21	67/28 42	33/12 20	—	82/40 58	15
9	22/5 12	33/8 18	75/25 40	45/20 30	—	75/32 48	16
10	25/5 13	35/10 18	50/15 27	23/10 15	—	60/15 33	19
11	22/10 14	27/12 16	40/17 25				
17	23/2 9	—	83/18 49				
18	22/7 12	24/12 16	50/25 38				
20	35/9 16	—	75/10 31				
Average of experimental animals	13 5	17.2	31.6	20.3	—	42.5	

*The data from Table III are rearranged according to the method of diversion of blood from the right lung (open chest vs. closed chest). Separate averages are shown for the two methods.

Fig. 4: The pulmonary artery pressures during right pulmonary artery occlusion tended to be higher in the animals with longer duration of atelectasis but there was considerable variation.

Histopathologic Study.—In general, the changes in the atelectatic lung were difficult to interpret because the alveolar spaces could not be distinguished. There was noticeable paucity of small blood vessels and blood-filled capillaries. Large macrophages were liberally scattered through the lung structures, both intra- and extrabronchially. The small bronchioles were collapsed and free of accumulated mucus. Only the larger bronchioles contained mucus. Hemosiderin deposits were scattered through the atelectatic tissue. Pleural thickening, while present, was minimal.

Representative photomicrographs of sections of normal and reaerated lungs are presented in Fig. 5.

The sections of reaerated lung after chronic atelectasis were revealing. The pleural surfaces were normal or minimally thickened. The subpleural zone of pulmonary parenchyma often seemed distinctly hypoinflated when compared to the remainder of the parenchyma. In this subpleural zone, the alveolar spaces were scarcely aerated whereas, in the remainder of the lung, there was overstretching of the terminal respiratory units and some disruption of alveolar walls. A number of prominent spurs or club-like processes were scattered through the lung. They were located particularly at the junction of bronchiolar arteries with perialveolar capillaries. The exact nature of these club-like processes is not known.

The sections of normal right lungs showed some enlargement of alveolar spaces and some disruption of alveolar septa.

DISCUSSION

These experimental data tend to confirm and reproduce the bronchospirometric observations in human beings of a ventilation-oxygen uptake discrepancy in reaerated chronically atelectatic lungs.

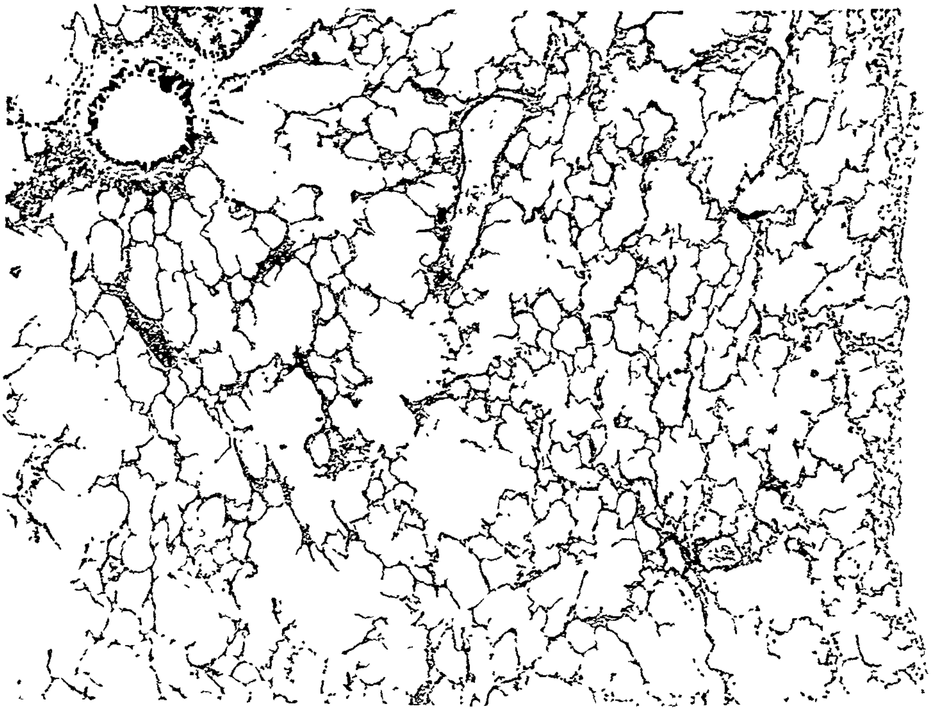


Fig. 5.—*A*, P8N. The right, unaffected lung shows some enlargement and minimal disruption of air spaces. (×56; reduced ⅓.)

Several investigators have measured the blood flow through an atelectatic left lung in the dog. They have reported a range from 0 to 40 per cent of cardiac output, with an average approximately 15 per cent.[2, 3, 4, 6, 10, 13, 14] A comparison with the present experimental observations of an average of 13.8 per cent of total oxygen uptake in the reaerated left lungs suggests that, while reaeration eliminates the shunt previously present,[3] it does not greatly improve the circulation through the lung.

This conclusion is supported by the pulmonary artery pressure data during temporary occlusion of the right pulmonary artery. It is clear that with pressures of more than 100 per cent over base line, these animals developed a considerable pulmonary hypertension. A similar right pulmonary artery occlusion in a normal animal results in less than 50 per cent elevation of base line pressure. The reaerated lungs were apparently unable to accommodate an acute and massive increase in blood flow because of increased pulmonary vascular resistance.

While there have been few reported human bronchospirometric studies after reaeration of a chronically atelectatic lung, there have been a number of reports of routine pulmonary function tests that have shown some increase in vital capacity after recovery. This increase has usually been small, presumably due to redistribution of approximately the same intrapleural volume from one lung preoperatively to two lungs postoperatively. While it was not possible to measure vital capacity in the present experimental animals with reaerated lungs, it is clear from chest roentgenograms (see Fig. 1) that a redistribution of pleural space took place when the atelectatic left lungs were reaerated. In addition, the separate hyperinflation of the reaerated lungs demonstrated that marked limitation existed in their compliance compared to the normal controls up to 2 years after reaeration. There is as yet no known reason for this reduction in compliance since previous histologic studies of atelectatic and reaerated lungs, in the absence of infection, have not shown pulmonary fibrosis or other change likely to result in decrease of pulmonary function. The diminished compliance must have been present at the reaeration operation to account for the smaller than normal size of the reaerated lungs. One observer reported that

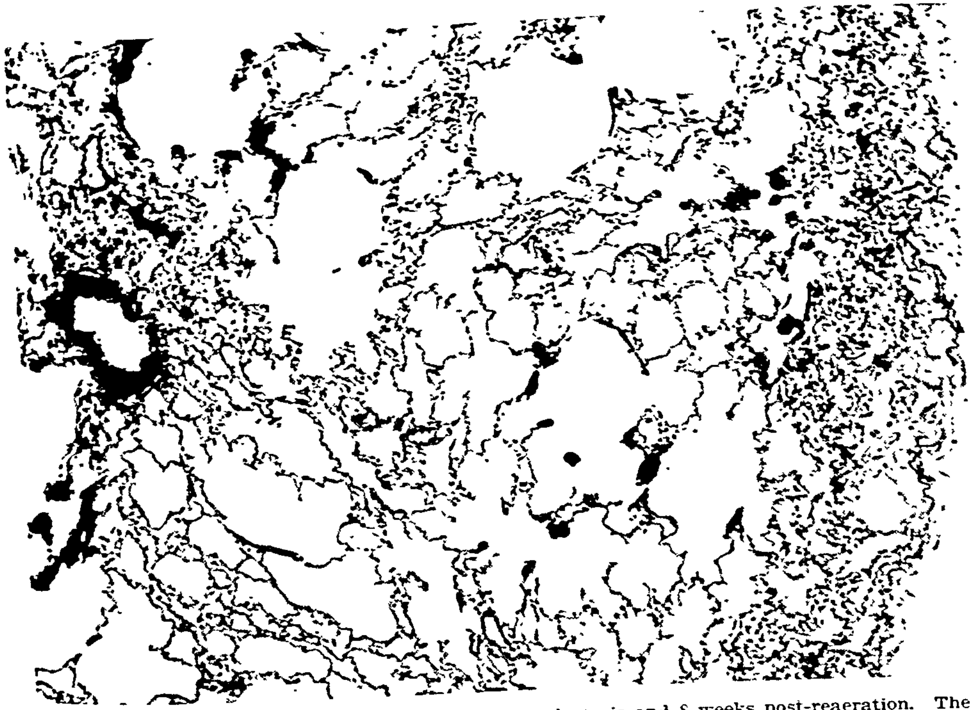


Fig. 5—Cont'd. *B*. P10N Eleven weeks of atelectasis and 8 weeks post-reaeration. The left, reaerated lung shows minimal thickening and infolding of the pleural surface. Note the subpleural zone of hypoinflation. There is some interalveolar septal thickening and frequent club-like formations at the junction of bronchiolar arteries with perialveolar capillaries. (×50; reduced 1/5.)

the reaerated lungs resumed normal size several weeks or months after reaeration.[9] The present study could not confirm this observation.

An increase in pulmonary arterial resistance with decrease in flow in one lung was produced experimentally by Rosenberg[15] by wrapping one lung in a constricting bag (i.e., a marked reduction of compliance). That the mechanism of the increased resistance and decreased flow is the same in the present experiment is not certain but highly suggestive. In addition, it corresponds with Benfield's observation that contralateral pneumonectomy was not tolerated. It is known that pneumonectomy in the normal dog is followed by little pulmonary artery pressure elevation if the remaining lung is free to make compensatory adjustments. The present data suggest that contralateral pneumonectomy forced cardiac output through a smaller than normal, compensation-limited, reaerated lung.[8] The resulting pulmonary hypertension was followed by right ventricle dilatation and hepatic congestion, and the pulmonary artery pressure probably exceeded the osmotic pressure of plasma protein which results in pulmonary edema, air hunger, and death. Carlson[5] suggested that edema could be caused by altered permeability of the alveolar-capillary membrane due to hypoxia during atelectasis but it is doubtful that such altered permeability would last significantly beyond the time of reaeration.

The present histopathologic findings in reaerated lungs of subpleural hypoinflation and bronchiolar arterial spur or club formation may be wholly or partially the cause of both the increased vascular resistance and diminished compliance. The significance of these changes is not yet fully understood.

The conservation of lung tissue stands as a worthy goal in patients afflicted with chronic atelectasis of one lung. It is known that surgical reaeration of these lungs will yield a number of physiologic benefits. The present study suggests that reaeration is useful but it may fall considerably short of restoring that lung to complete normality. This statement is not an implied disagreement with the policy of surgical reaeration of atelectatic lungs but rather a suggestion that patients who have undergone reaeration operations be studied fluoroscopically, bronchospirometrically, and hemodynamically, as in the present study, whenever possible. The results of these and other follow-up studies will help to define the full clinical significance of the altered hemodynamics in the pulmonary circulation following reaeration of an atelectatic lung.

CONCLUSIONS

1. Reaeration of a chronically atelectatic lung in the dog restores its function partially. However, specific physiologic defects remain. They include a variable but persistent loss of compliance, a marked increase in pulmonary vascular resistance, a diminished pulmonary artery blood flow, and a concomitant decrease in oxygen uptake.

2. Histopathologic changes have been noted in reaerated atelectatic animal lungs. A zone of subpleural hypoinflation was noted. Bronchiolar arteries exhibited formation of spurs or club-like processes. The significance of the changes is not yet clear.

3. In human beings with a reaerated chronically atelectatic lung, a similar partial restoration of function with decrease in oxygen uptake has been reported by others.

4. From the published reports of some patients it appears that the passage of time has favorably influenced the function of reaerated atelectatic lungs. Such a favorable influence of time could not be confirmed in the present experimental study.

5. It is suggested that a complete functional evaluation of a patient with a reaerated lung after chronic atelectasis might properly include bronchospirometry and an investigation of vascular resistance and pulmonary compliance.

SUMMARY

The pulmonary functions and cardiac output of 10 dogs were studied during bronchospirometry after reaeration of a chronically atelectatic left lung.

The pulmonary arterial pressure response of 20 dogs was studied during temporary occlusion of the right pulmonary artery after reaeration of a chronically atelectatic left lung.

Normal, atelectatic, and reaerated lungs were compared histopathologically.

REFERENCES

1. Adams, W. E.: Detailed Description of a Safe and Reliable Method for Closing Large Bronchi, J. Thoracic Surg. 3: 198-200, 1933.
2. Andrus, W. de W.: Observations on the Cardio-respiratory Physiology Following the Collapse of One Lung by Bronchial Ligation, Arch. Surg. 10: 506, 1925.
3. Benfield, J. R., Long, E. T., Harrison, R. W., Perkins, J. W., Jr., Herman, G. P., and Adams, W. E.: Should a Chronic Atelectatic Lung Be Reaerated or Excised? Dis. Chest 37: 67-74, 1960.
4. Björk, V. O., and Salen, E. F.: The Blood Flow Through an Atelectatic Lung, J. Thoracic Surg. 20: 939, 1950.
5. Carlson, R. I., Classen, K. L., Gollan, F., Gobbel, W. G., Jr., Sherman, D. E., and Christensen, R. O.: Pulmonary Edema Following the Rapid Re-expansion of a Totally Collapsed Lung Due to Pneumothorax. A Clinical and Experimental Study, S. Forum 9: 367, 1958.
6. Coryllos, P. N., and Birnbaum, G. K.: The Circulation in the Compressed, Atelectatic and Pneumonic Lung, Arch. Surg. 19: 1346, 1929.
7. Forster, E.: Atelectasie pulmonaire prolongee et reversibilite functionelle, Lyon chir. 52: 484-487, 1956.
8. Gerst, P. H., Rattenborg, C., and Holaday, D.: The Effects of Reduced Pulmonary Blood Flow on Pulmonary Circulation and Respiratory Gas Exchange, S. Forum 9: 374-378, 1958.
9. Hinshaw, J. R., and Emerson, G. L.: Histologic Studies of the Lung During Recovery From Atelectasis, S. Forum 9: 390-392, 1958.
10. Keeley, J. L., and Gibson, J. G.: Experimental Atelectasis in Dogs, Surgery 11: 527, 1942.
11. Loosli, C. G., Adams, W. E., and Thornton, T. M., Jr.: The Histology of the Dog's Lung Following Experimental Collapse, Anat. Rec. 105: 697-721, 1949.
12. Mahaffey, D. E., Creech, O., Jr., and De Bakey, M. E.: Traumatic Rupture of the Left Main Bronchus Successfully Repaired Eleven Years After Injury, J. Thoracic Surg. 32: 312-331, 1956.
13. Moore, R. L.: The Volume of Blood Flow per Minute Through the Lungs Following Collapse of One Lung by Occlusion of Its Bronchus, Arch. Surg. 22: 225, 1931.
14. Peters, R. M., Loring, W. E., and Sprunt, W. H.: An Experimental Study of the Effect of Chronic Atelectasis on Pulmonary and Bronchial Blood Flow, Circulation Res. 7: 31-36, 1959.

15. Rosenberg, M. Z.: Effects of Unilateral Collapse of the Lung, Yale J. Biol. & Med. 25: 51, 1952.
16. Samson, P. C.: Discussion of Mahaffey, Creech, and De Bakey.[12]
17. Webb, W. R., and Burford, T. H.: Studies of the Re-expanded Lung After Prolonged Atelectasis, A. M. A. Arch. Surg. 66: 801-809, 1953.
18. Webb, W. R., and Smith, J. R.: Pulmonary Hemodynamics as Affected by Varying Levels of Respiratory Pressure, S. Forum 9: 371-374, 1958.
19. Weisel, W., and Jake, R. J.: Anastomosis of Right Bronchus to Trachea 46 Days Following Complete Bronchial Rupture From External Injury, Ann. Surg. 137: 220-227, 1953.

(For Discussion, see page 699)

SELECTIVE CHEMOTHERAPY OF THE LUNG DURING UNILATERAL PULMONARY ARTERIAL OCCLUSION WITH A BALLOON-TIPPED CATHETER

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The use of pulmonary intra-arterial carcinolytic agents, administered either by trapping in the lung or by selective perfusion of the lung, has been previously reported.[1, 2] Clinical application of these techniques is hampered if a carcinoma involves the hilum of the lung, preventing access to the pulmonary artery.

Perhaps the greatest problem in selective chemotherapy of the lung is that, while the pulmonary arterial system is suitable for isolation-perfusion techniques, the great majority of pulmonary diseases, including primary bronchogenic carcinoma, apparently derive their blood supply from the bronchial arterial system.[3-12] Metastatic tumors are probably supplied by the pulmonary arterial system.[6, 12]

In the normal lung, there are both capillary and dormant precapillary communications between the two arterial systems.[11, 13-16] In the presence of primary bronchogenic carcinoma, bronchiectasis, tuberculosis, and many other diseases, extensive functioning precapillary communications develop between the two arterial systems.[3-8, 10-12] It is natural to suppose that these are left-to-right shunts.

In support of this are the findings of increased oxygen saturation of the pulmonary arterial blood in the vicinity of primary carcinoma and other diseases[5, 7, 8, 9, 17]; the failure of pulmonary angiograms to fill the pulmonary arteries in the vicinity of disease[7, 18]; and the finding of left ventricular hypertrophy in such cases.[17, 19-22]

Against this are the findings of Brofman[23] and Nemir,[24] and their associates, who used a balloon-tipped cardiac catheter to occlude the right or left pulmonary artery in the study of lung function. They found that the pressure in the pulmonary artery, distal to the occlusion, fell to pulmonary capillary levels even in the presence of extensive bronchiectasis, a disease associated with marked increase in bronchial-pulmonary arterial anastomoses. The higher

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pressures expected from bronchial arterial precapillary inflow were not encountered. Furthermore, the oxygen saturation of this "lacunar" blood was higher than that of the systemic blood and the pulmonary capillary blood, indicating that it was derived not from bronchial arterial inflow but, rather, from left atrial reflux; that is, blood that had passed through the pulmonary capillary bed twice.

These discrepancies are not easily reconciled, but it appears that during unilateral pulmonary arterial occlusion, perhaps as a result of some neurogenic mechanism, significant left-to-right precapillary bronchial-pulmonary arterial shunts do not occur.[23]

It seemed to us that under these conditions, it might be possible to reach both primary and metastatic tumors with a chemotherapeutic agent injected into the pulmonary artery distal to its occlusion by a balloon-tipped cardiac catheter. This technique would have the further advantages of allowing access to a pulmonary artery involved by tumor and selective, and possibly repeated, chemotherapy of the lung without thoracotomy.

The circulation and diffusion of indicator substances and the tolerance of the lung for various doses of nitrogen mustard were studied in the dog during unilateral pulmonary arterial occlusion, prior to a clinical trial of the method. Based on the observation of Creech and associates[25] that fixation or inactivation of nitrogen mustard occurs within 8 minutes in whole blood, an occlusion time of 15 minutes was arbitrarily chosen.

METHODS

1. *Circulation.*—The circulation in the lung was studied in mongrel dogs, weighing 15 to 25 kilograms, that were divided into four groups.

Group 1: A control group in which the pulmonary artery was not occluded.
Group 2: Animals in which the right pulmonary artery was occluded.
Group 3: Animals in which the right pulmonary artery and the right bronchial artery were occluded.
Group 4: Animals in which the right pulmonary artery, the right bronchial artery, and the right main stem bronchus were occluded.

The animals were anesthetized with intravenous Pentothal sodium. Oxygen was administered by intermittent positive pressure of 14 cm. of water through a cuffed endotracheal tube. Either a No. 8½ Fr. double lumen balloon-tipped cardiac catheter* or a No. 7 Fr. single lumen cardiac catheter was inserted through the right external jugular vein and positioned in the right pulmonary artery at right thoracotomy. The pulmonary artery was occluded either by inflating the balloon or by the use of a snare (Fig. 1). In Groups 3 and 4, the bronchial arterial inflow was occluded by skeletonizing the hilum and dividing all small vessels on the isolated bronchus. In Group 4, the bronchus was occluded by a non crushing clamp.

T 1824 (Evan's blue dye) and a saline suspension of Cr^{51} tagged red blood cells were used as indicators. To minimize errors in either method, both indicators were used simultaneously in each experiment. Indicator dilution curves were obtained in 5 animals weighing 20 to 25 kilograms in each group. Two milliliters of each indicator were slowly injected through the catheter over a 2 minute period to permit adequate diffusion in the lung. Blood samples were obtained through a Cournand needle in the femoral artery.

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*Dotter-Lukas No 1, U S Catheter & Instrument Corp, Glens Falls, N Y The standard balloon was replaced by a smaller one for animal experiments

In the control group, samples were taken at 1, 5, 10, and 20 minutes after completion of the injection. In Groups 2, 3, and 4, the injection was started 2 minutes after pulmonary arterial occlusion, a time arbitrarily chosen to permit stabilization of the circulation. Blood samples were taken at intervals of 1 minute, 3 minutes, 5 minutes, and 10 minutes after completion of the injection. The occlusion was then released, and further samples taken 1 minute and 10 minutes later. Complete mixing was assumed to have taken place at this time and the readings for the last sample were taken to represent 100 per cent of the indicator in the systemic circulation in each experiment.

The values for T 1824 were obtained by a modification of the method of Hamilton and associates,[26] using the Beckman DU spectrophotometer. The values for Cr^{51} tagged red blood cells were obtained by a modification of the method of Spencer and associates.[27] To correct for varying radioactivity in different preparations of Cr^{51} tagged red blood cells, all readings were corrected to a uniform standard of 2.75 million counts per milliliter per 5 minutes.

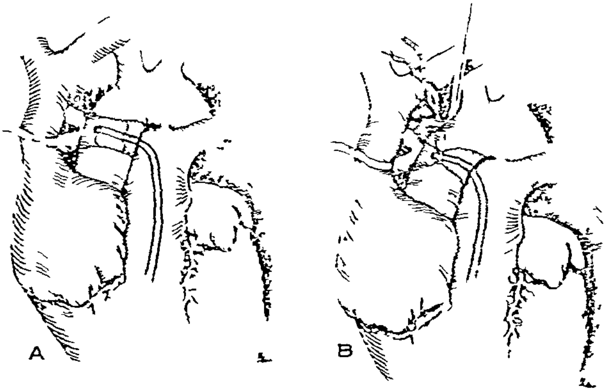

Fig 1.—Methods used to occlude the pulmonary artery. *A* Balloon-tipped double lumen cardiac catheter. *B* Single lumen cardiac catheter with a snare around the pulmonary artery.

Since the behavior of inert indicators could only approximate that of a highly reactive agent like nitrogen mustard, their exact concentration in the blood was not important. We were only interested in what percentage of the total amount, if any, appeared in the systemic circulation during pulmonary arterial occlusion. A simple linear projection was therefore used in plotting the dilution curves rather than the conventional semi logarithmetical projection, and the data were plotted as units of optical density and counts per milliliter per 5 minutes, against time in minutes.

2. *Diffusion*.—The distribution of an indicator was also studied in 5 animals, weighing 15 to 20 kilograms, in each group. Five milliliters of methylene blue dye were injected through the catheter, and the time of appearance, the distribution, and the duration of the blue stain studied.

3. *Dose of Nitrogen Mustard*.—The tolerance of the lung for nitrogen mustard was studied in 14 animals, weighing 15 to 20 kilograms. Under intravenous Pentothal sodium anesthesia, a No. 8½ Fr balloon tipped double lumen cardiac catheter was inserted into the external jugular vein and positioned in the right or left pulmonary artery, under fluoroscopic control in 9 animals and, at right thoracotomy, in 5 animals. The balloon was inflated with 50 per cent Hypaque* until the pulmonary arterial pressure distal to the balloon fell to pulmonary capillary levels. A solution of nitrogen mustard in saline (1.0 mg per milliliter) was then injected into the blood stream distal to the balloon, in doses of 0.1, 0.2, 0.3, or 0.4 mg per kilogram, during a period of 15 minutes of occlusion.

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*Winthrop Laboratories, New York, N. Y.

On each animal, white blood cell, hematocrit, and platelet counts were obtained before the perfusion and at weekly intervals thereafter. Chest roentgenograms were obtained before and 24 hours after the perfusion, and at weekly intervals thereafter.

In a control group of 5 animals, a dose of nitrogen mustard of 0.4 mg. per kilogram was given intravenously. White blood cell, hematocrit, and platelet counts were obtained on each animal before the injection of nitrogen mustard, and at weekly intervals thereafter.

All the animals were observed for a period of 4 weeks.

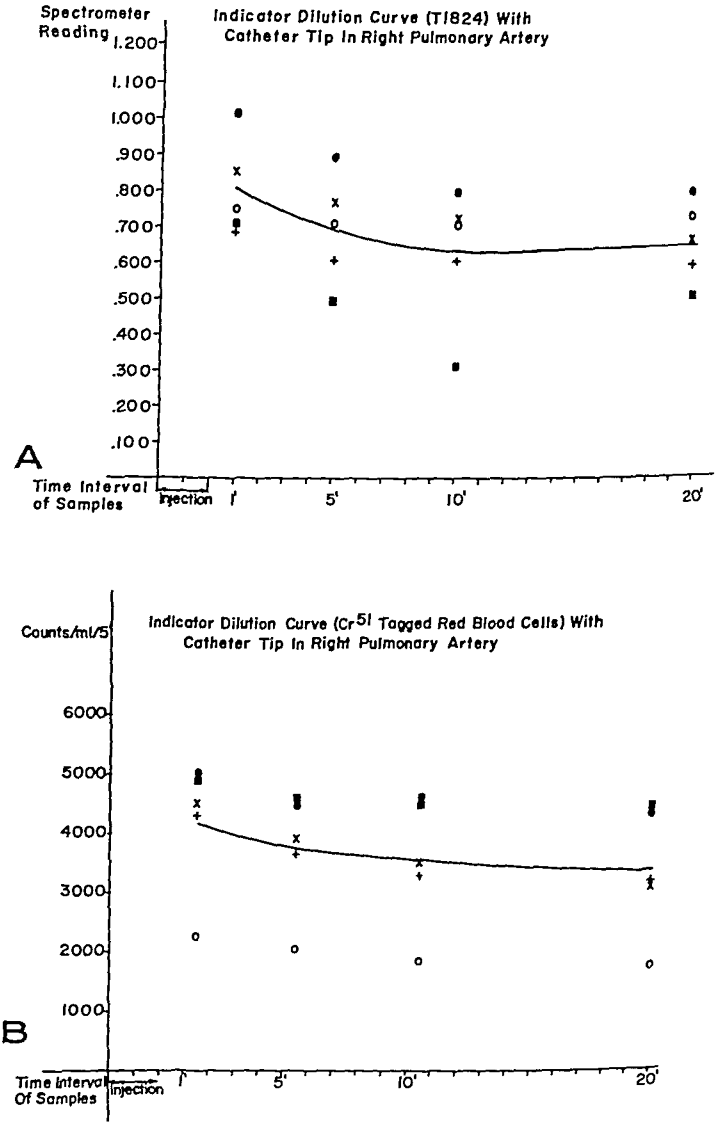


Fig. 2.—Indicator dilution curves in the control group. *A*, T-1824. *B*, Cr^{51} tagged red blood cells.

RESULTS

1. *Circulation of Indicator.*—In the control group, both indicators appeared immediately in the peripheral circulation in concentrations that declined from an initial high level to a lower plateau, 10 to 20 minutes after injection (Fig. 2).

In each group of the test series, the indicator dilution curves showed a delay in passage of the indicators through the lung, with a progressive leak into the systemic circulation. On releasing the pulmonary arterial occlusion, the indicator trapped in the lung was washed out into the systemic circulation, producing a sharp rise in concentration of the indicator, which then fell slightly to control levels as mixing occurred during the next 10 minutes.

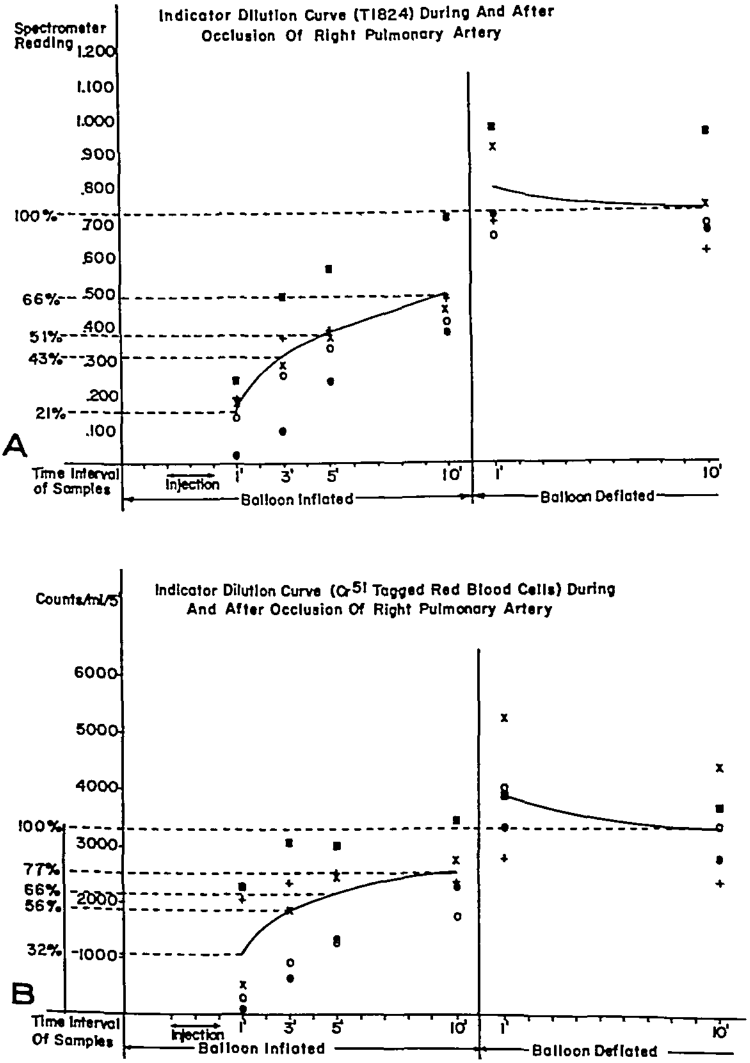


Fig. 3.—Indicator dilution curves in Group 2. *A*, T-1824. *B*, Cr^{51} tagged red blood cells. The linear plot allows the pulmonary-systemic leak to be expressed as a percentage of the total amount in solution, represented by the value 10 minutes after release of pulmonary arterial occlusion.

In Group 2, taking the average of values obtained with both indicators, the amount of the indicator reaching the systemic circulation at 1, 3, 5, and 10 minutes after injection was 26 per cent, 49 per cent, 58 per cent, and 71 per cent, On each animal, white blood cell, hematocrit, and platelet counts were obtained before the perfusion and at weekly intervals thereafter. Chest roentgenograms were obtained before and 24 hours after the perfusion, and at weekly intervals thereafter.

In a control group of 5 animals, a dose of nitrogen mustard of 0.4 mg. per kilogram was given intravenously. White blood cell, hematocrit, and platelet counts were obtained on each animal before the injection of nitrogen mustard, and at weekly intervals thereafter.

All the animals were observed for a period of 4 weeks.

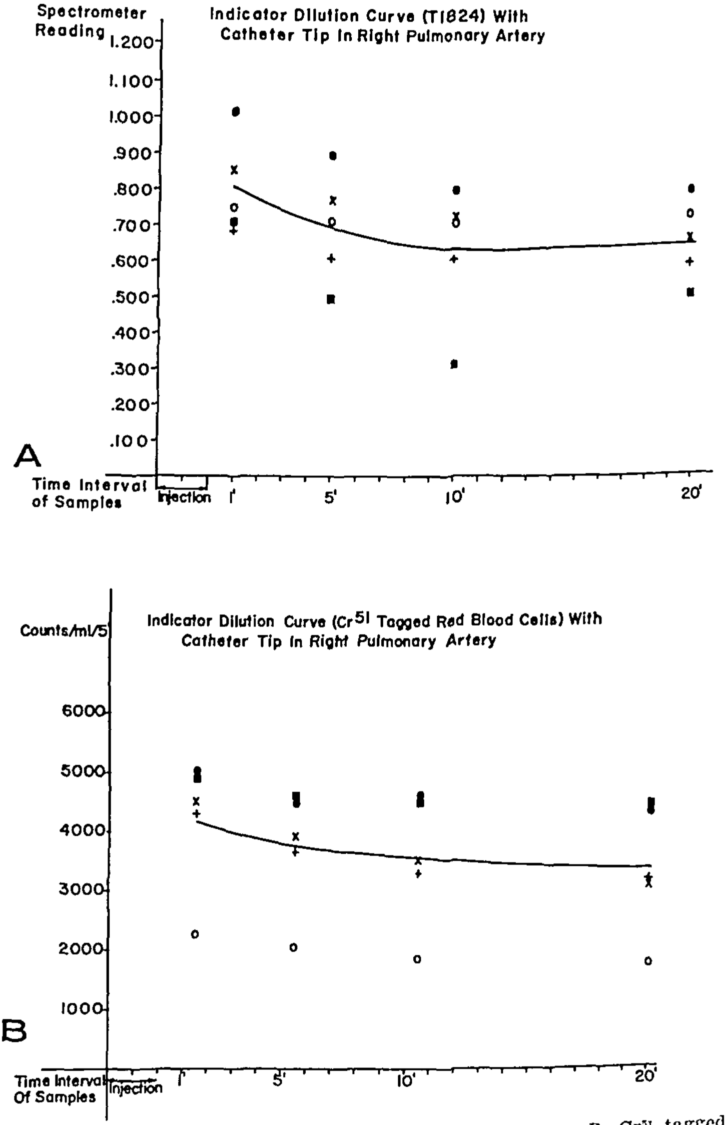


Fig. 2.—Indicator dilution curves in the control group *A*, T-1824. *B*, Cr^{51} tagged red blood cells.

RESULTS

1. *Circulation of Indicator.*—In the control group, both indicators appeared immediately in the peripheral circulation in concentrations that declined from an initial high level to a lower plateau, 10 to 20 minutes after injection (Fig. 2).

In each group of the test series, the indicator dilution curves showed a delay in passage of the indicators through the lung, with a progressive leak into the systemic circulation. On releasing the pulmonary arterial occlusion, the indicator trapped in the lung was washed out into the systemic circulation, producing a sharp rise in concentration of the indicator, which then fell slightly to control levels as mixing occurred during the next 10 minutes.

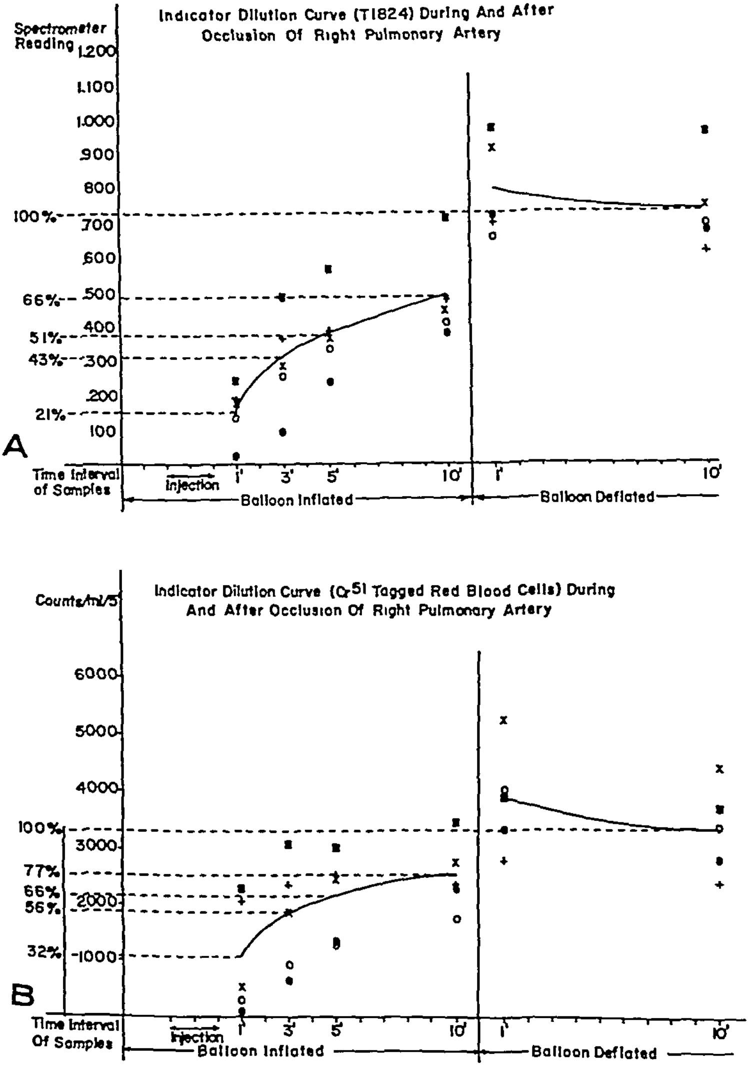


Fig. 3—Indicator dilution curves in Group 2 *A*, T-1824 *B*, Cr^{51} tagged red blood cells The linear plot allows the pulmonary-systemic leak to be expressed as a percentage of the total amount in solution, represented by the value 10 minutes after release of pulmonary arterial occlusion

In Group 2, taking the average of values obtained with both indicators, the amount of the indicator reaching the systemic circulation at 1, 3, 5, and 10 minutes after injection was 26 per cent, 49 per cent, 58 per cent, and 71 per cent, respectively (Fig. 3). In the remaining groups, the pulmonary-systemic leak was slightly smaller: the corresponding values being 26, 38, 44, and 65 per cent in Group 3, and 23, 34, 50, and 64 per cent in Group 4.

2. *Diffusion of Indicator.*—In the control group, the methylene blue stain appeared in the visceral pleura of all lobes of the lung within seconds of starting the injection. A uniform blue stain of maximum density was present at the end of the injection period, or within 2 minutes of completion of the injection. It began to fade at once and, 15 minutes after the injection, only a trace of the blue stain remained.

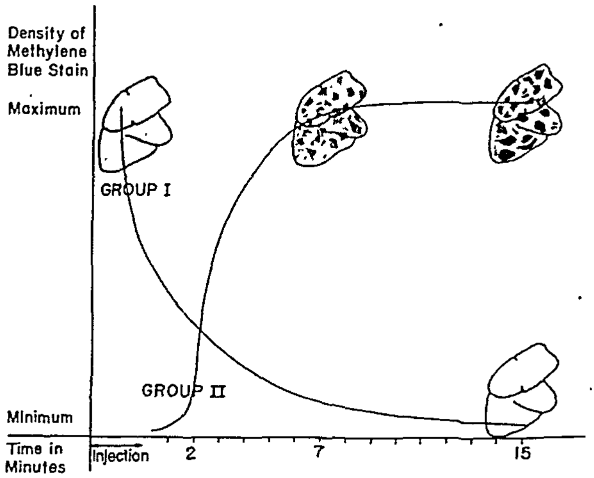


Fig. 4.—Schematic drawing which contrasts the even staining and rapid fading of the dye in the control group, with the slower, less uniform, but more persistant staining of the dye in the test series.

In the test series, the picture was quite different. In each group, the blue stain first appeared within 2 minutes of the end of the injection in all lobes, in patchy areas that stained more deeply than in the control group. A more uniform stain of lesser density then appeared, to reach a maximum 7 or 8 minutes after injection. There was no fading of the stain during the remainder of the 15-minute period of pulmonary arterial occlusion. There was no apparent difference in the distribution pattern of the dye between Groups 2, 3, and 4. The blue stain was never as uniform, either in density, or distribution, as in Group 1, the control series (Fig. 4).

3. *Effect of Nitrogen Mustard.*—In the control series, all the animals survived the 4-week observation period. All developed transient anorexia, diarrhea, weight loss, and moderate leukopenia.

In the test series, none of the animals developed leukopenia. All the animals survived a dose of nitrogen mustard of 0.1 mg. or 0.2 mg. per kilogram. Only 1 animal survived a dose of 0.3 mg. per kilogram, and 1 a dose of 0.4 mg. per kilogram. Both of these developed transient anorexia, diarrhea, and weight loss.

All the animals developed roentgenographic evidence of pneumonitis or atelectasis within 24 hours of lung perfusion (Fig. 5). Roentgenographically there was no correlation between its extent, severity, or duration and the dose of nitrogen mustard. The pneumonitis cleared in 1 to 4 weeks in all but 2 animals.

CLINICAL EXPERIENCE

Right heart catheterization was performed four times on 3 patients. A No. 8½ Fr. Dotter-Lukas balloon-tipped double lumen cardiac catheter was introduced into a peripheral vein and positioned in the right or left pulmonary artery under fluoroscopic control. In 1 patient, a second catheter was inserted to record pressures proximal to the balloon. A Cournand needle was placed in the brachial artery.

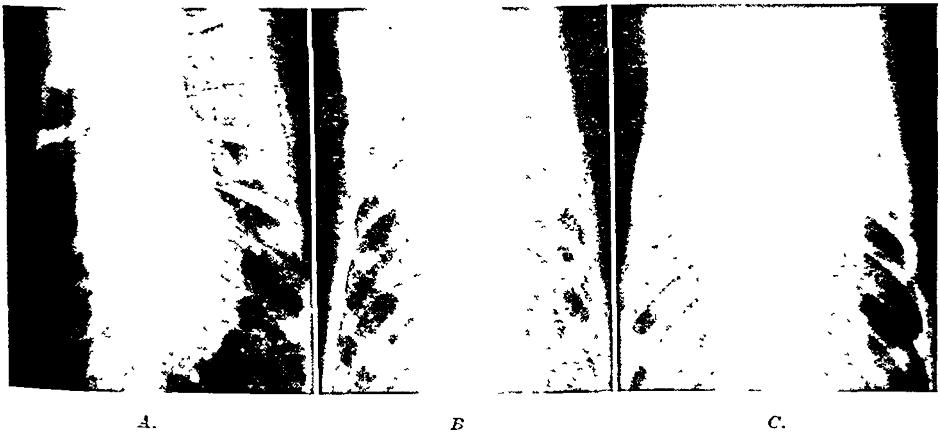


Fig. 5.—Roentgenograms of dog's chest. A, Before perfusion. B, During perfusion with the balloon catheter in position in the right pulmonary artery. C, Twenty-four hours later; showing severe penumonitis and atelectasis of the right upper lobe.

The balloon was inflated with 50 per cent Hypaque until the pulmonary artery pressure fell to pulmonary capillary levels (Figs. 6 and 7). Indicator dilution curves were then obtained by the method described, using 2 ml. of T-1824.

The balloon was then reinflated and the calculated dose of nitrogen mustard administered. Occlusion of the pulmonary artery was maintained for 15 minutes.

CASE REPORTS

Case 1.—A dose of 0.1 mg. per kilogram of nitrogen mustard (7.5 mg. in 7.5 ml. of saline) was administered by this technique to a 54-year-old man with an inoperable epidermoid carcinoma of the right lower lobe, metastatic to the thyroid gland. A moderately severe pneumonitis developed within 24 hours. The patient remained asymptomatic and afebrile. Roentgenograms of the chest were made frequently until the patient's death 2 months later. There was no evidence of reduction in the size of the tumor. The pneumonitis did not completely clear (Fig. 8).

CASE 2.—A dose of 0.05 mg. per kilogram of nitrogen mustard (3.4 mg. in 6.8 ml. of saline) was administered to a 22-year-old man with bilateral pulmonary metastases from an osteogenic sarcoma of the right femur. Amputation had been performed a year previously. The left lung was perfused first and the right a month later. A mild perihilar pneumonitis that cleared in 48 hours appeared after the first perfusion. No pneumonitis was noted after the second perfusion. Following the first perfusion, the lesions in the left lung remained static with the exception of two that increased slightly in size in contrast to the rapid progression of those in the right lung (Fig. 9). Follow-up chest roentgenograms have not yet been obtained following perfusion of the right lung.

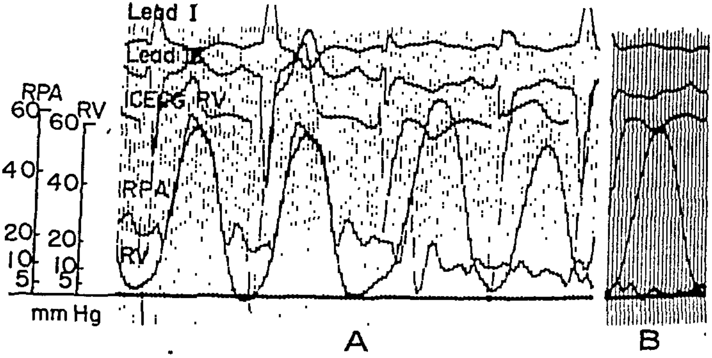
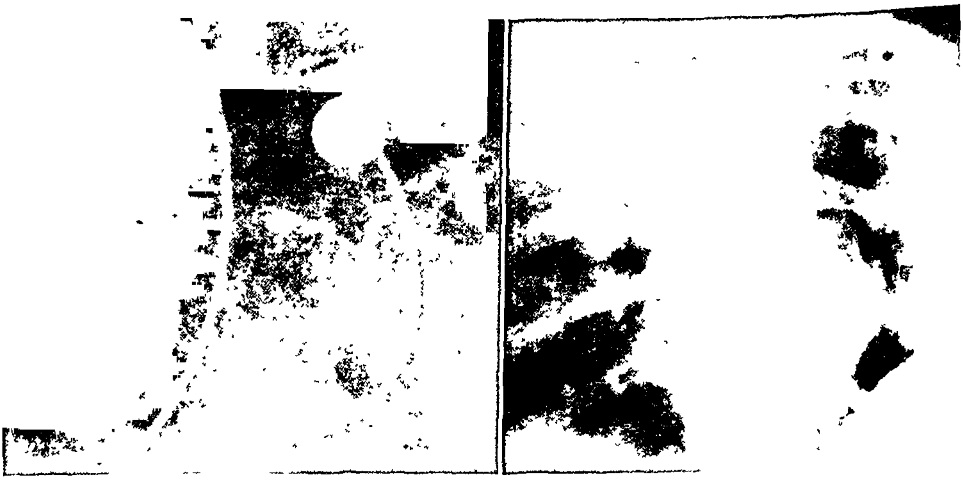


Fig. 6.—Case 3. [illegible] and pressure data recorded at paper speed of 75 mm. per second. Time [illegible] second. *A*, At the moment of pulmonary arterial occlusion by the inflate [illegible] seconds later. The data show right bundle branch block and pulmonary hypertension. The pulmonary arterial pressure drops immediately to normal pulmonary capillary levels when occlusion of the artery is complete.



A. *B.*

Fig. 7.—*A*, Balloon catheter in left pulmonary artery. The balloon is seen end-on as the artery arches over the left main-stem bronchus. *B*, Balloon catheter in the right pulmonary artery. Here the balloon lies transversely and has a characteristic "sausage" shape when occlusion of the artery is complete.

CASE 3.—A dose of 0.1 mg. per kilogram of nitrogen mustard (5.1 mg. in 5.1 ml. of saline) was administered to a 65-year-old man with an inoperable adenocarcinoma of the right lung, metastatic to the scalene nodes (Fig. 10, *A*). On admission to the George Washington University Hospital, the patient had developed partial atelectasis of the middle and lower lobes and a large pleural effusion, with roentgenographic evidence of lymphatic

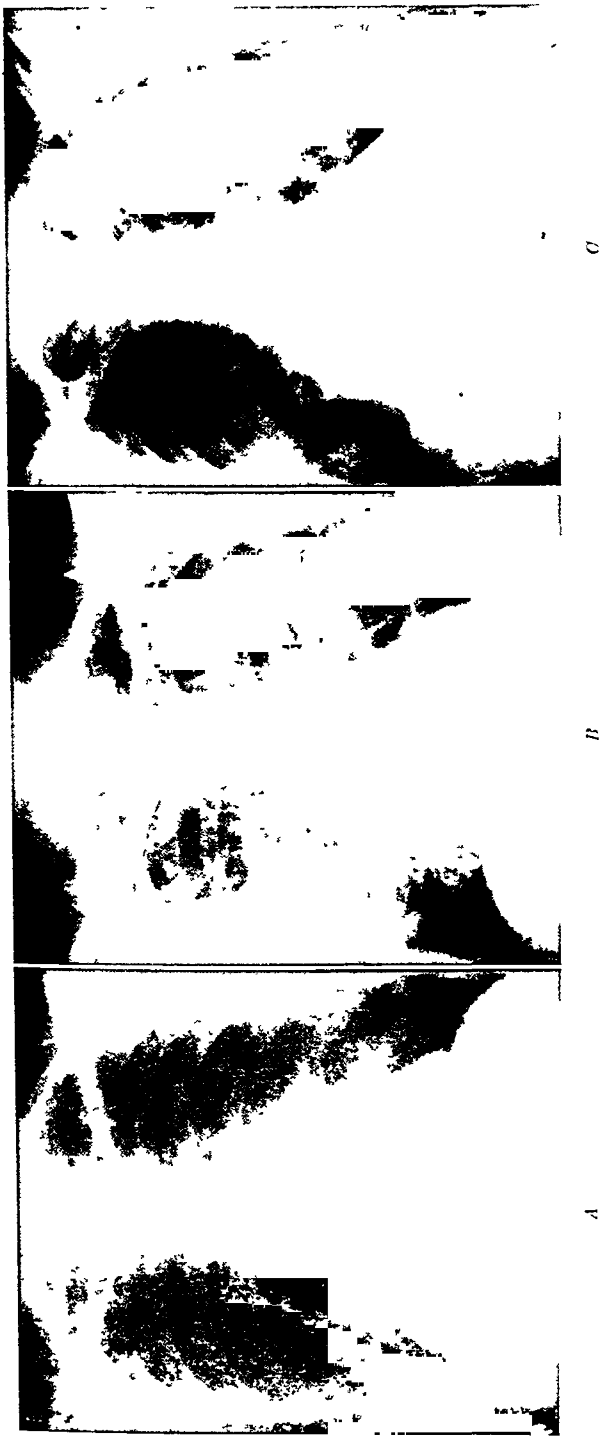


Fig 8 —Case 1 Roentgenograms of the chest. *A*, Before perfusion. *B*, Twenty-four hours after perfusion *C*, Two months after perfusion.

spread of the tumor throughout the right lung (Fig. 10, *B*). Thoracentesis on two occasions yielded small amounts of serosanguineous fluid. Examination for malignant cells was reported as grade 3 on the first specimen and negative on the second. Following the perfusion, the effusion rapidly absorbed and had not recurred at the time of the last follow up roentgenogram made 6 weeks later (Fig. 10, *C*). Compared with the first, this last roentgenogram showed the parahilar mass to be slightly smaller; there was reaeration of the middle and lower lobes with persistent minimal pneumonitis, probably caused by the nitrogen mustard.

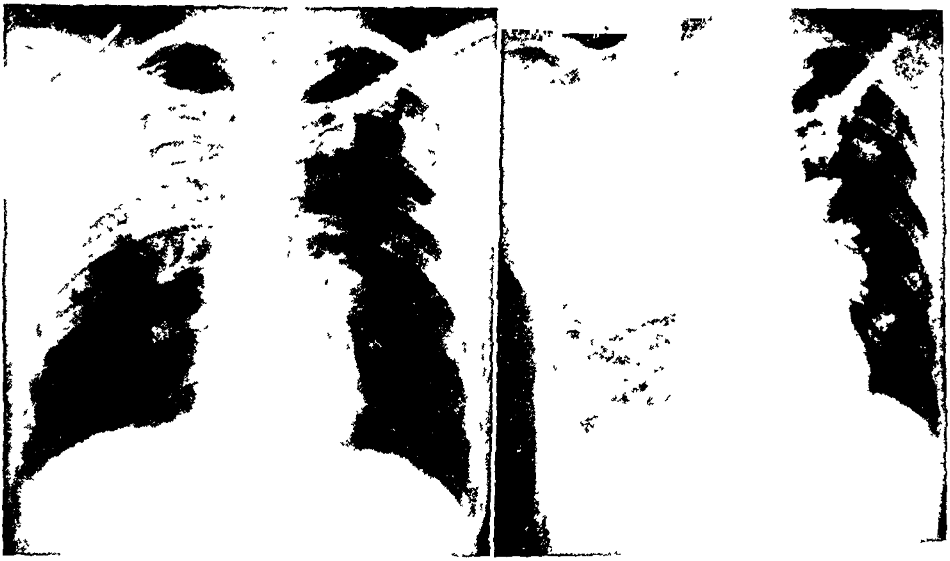


Fig 9.—Case 2 Roentgenograms of the chest *A*, Before perfusion *B*, One month after perfusion of the left lung

DISCUSSION

These data show that an indicator substance, injected into the pulmonary artery distal to its occlusion, slowly diffuses throughout the lung and is gradually released into the systemic circulation, presumably as a result of eddy currents due to variations in the left atrial pressure In the normal dog's lung, bronchial arterial flow and respiratory movements contribute very little to this circulatory pattern.

In our patients, as in those of Brotman[2] and Nemir[24] and their associates, the distal pulmonary arterial pressure fell to normal pulmonary capillary levels on inflation of the balloon (see Fig 6). Oxygen studies on the last patient showed the saturation of this "lacunar" blood to be higher than that of the systemic blood. However, the indicator dilution curves in all 3 patients showed a substantially greater pulmonary-systemic leak than that found in the experimental animals (Fig. 11) Increased bronchial arterial flow in the presence of disease, without change in "lacunar" pressure, is a possible explanation, although this would not be expected in the presence of metastatic disease. Further study is needed to clarify this discrepancy

The slow circulation and somewhat uneven distribution of the indicator explain the lower tolerance of the lung for nitrogen mustard administered in

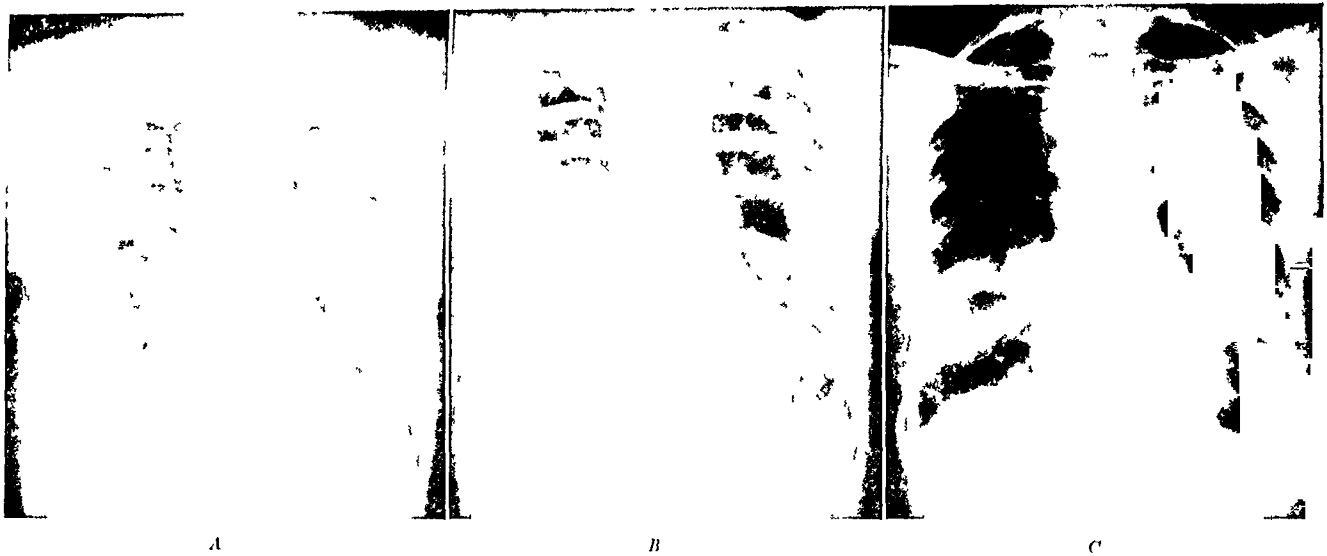


Fig. 10.—Case 3. Roentgenograms of the chest. A, One week before perfusion showing the right parahilar tumor, widening of the superior mediastinum and minimal right pleural effusion. B, The day before perfusion, showing a large pleural effusion with partial atelectasis of the underlying middle and lower lobes. C, Six weeks after perfusion; the fluid has almost completely absorbed. There is aeration of the underlying lung and the primary tumor is slightly smaller.

this manner than is found with isolated perfusion, which permits the safe administration of a dose of 0.4 mg. per kilogram.[2]

Study of the perfused dog's lung at autopsy showed that the acute pulmonary lesion produced by the nitrogen mustard, and interpreted roentgenographically as pneumonitis, was actually hemorrhagic necrosis of the lung. The chronic lesion in the human lung (Case 1) was found at autopsy to be anemic infarction secondary to widespread thrombosis of small pulmonary arteries. Neither lesion showed any inflammatory component.

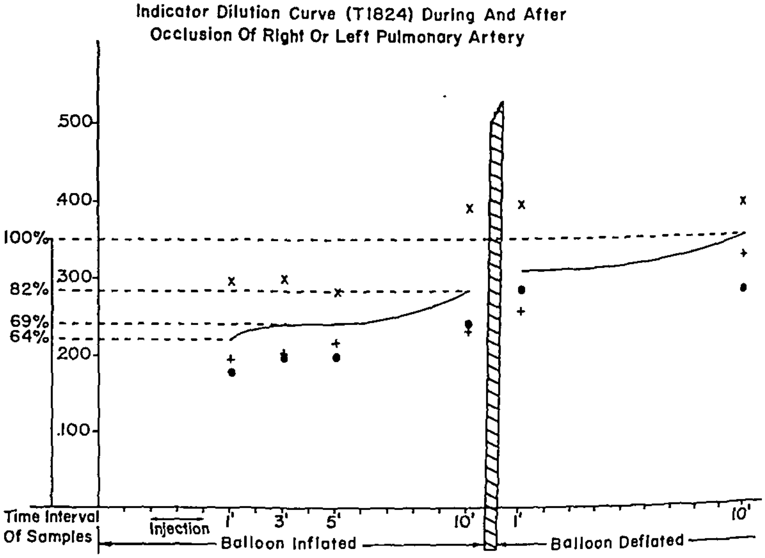


Fig. 11.—Cases 1, 2, and 3. Indicator dilution curve with T-1824.

The contrast in survival rate between the control and the test series of animals receiving nitrogen mustard, in a dose of 0.4 mg. per kilogram, suggests that the effect of the drug on the lung is the limiting factor in dosage rather than the size of the pulmonary-systemic leak. Experimental data suggest the maximum dose of nitrogen mustard to be 0.2 mg. per kilogram. Clinical experience, however, suggests that the maximum permissible dose may be 0.1 mg. per kilogram.

On a comparative weight basis (a lung to total body ratio of 1:150), allowing for the leak into the systemic circulation, a dose of nitrogen mustard administered in this way should provide a tissue concentration some fifty to one hundred times that obtainable by intravenous injection.

The results of treatment in 2 of the 3 patients are encouraging. Further study of this method, both with nitrogen mustard and other chemotherapeutic agents, such as 5-fluorouracil, is being undertaken.

SUMMARY

The circulation in the lung during unilateral pulmonary arterial occlusion by a balloon-tipped cardiac catheter has been studied in the dog and in man.

Studies with various indicators show widespread, slightly uneven, diffusion throughout the lung with a progressive leak into the systemic circulation.

The tolerance of the lung for nitrogen mustard administered by this technique is the limiting factor in dosage rather than the size of the pulmonary-systemic leak.

Nitrogen mustard, in doses of 0.05 to 0.1 mg. per kilogram, was safely injected into the pulmonary artery distal to its occlusion, with beneficial effect on primary and metastatic tumors in 2 of 3 patients.

This technique allows repeated chemotherapy of the lung without thoracotomy, is selective within limits, and, on a comparative weight basis (lung to total body), should provide a tissue concentration of nitrogen mustard fifty to one hundred times that obtainable by intravenous injection.

The assistance, in the indicator dilution studies, of Dr. George Kelser of the Department of Medicine and Dr. Ramsey MacCordy of the Department of Anesthesiology is gratefully acknowledged.

REFERENCES

1. Blades, B. B., and Hall, E. R.: Preliminary Observations on the Injection of Potentially Carcinolytic Drugs Into the Pulmonary Artery With Temporary Occlusion of the Blood Supply to the Lung, Am. Surgeon 24: 492, 1958.
2. Pierpont, H., and Blades, B.: Lung Perfusion With Chemotherapeutic Agents, J. THORACIC SURG. 39: 159, 1960.
3. Crockett, F. B., and Vass, C. C. N.: A Comparison of the Role of the Bronchial Arteries in Bronchiectasis and in Experimental Ligation of the Pulmonary Artery, Thorax 6: 268, 1951.
4. Liebow, A. A., Hales, M. R., Bloomer, W. E., Harrison, W., and Lindskog, G. E.: Studies on the Lung After Ligation of the Pulmonary Artery, Am. J. Path. 26: 177, 1950.
5. Liebow, A. A., Hales, M. R., Bloomer, W., and Lindskog, G. E.: The Genesis and Functional Implications of Collateral Circulation of the Lungs, Yale J. Biol. & Med. 22: 637, 1950.
6. Wood, D. C., and Miller, M.: The Role of the Dual Pulmonary Circulation in Various Pathologic Conditions of the Lungs, J. THORACIC SURG. 7: 649, 1938.
7. Cudcowicz, L., and Wraith, D. G.: A Method of Study of the Pulmonary Circulation in Finger Clubbing, Thorax 12: 313, 1957.
8. Roosenburg, J. G., and Deenstra, H.: Bronchial-Pulmonary Vascular Shunts in Chronic Pulmonary Infections, Dis. Chest 26: 664, 1954.
9. Gilroy, J. C., Wilson, V. H., and Marchand, P.: Observations on the Hemodynamics of Pulmonary and Lobar Atelectasis, Thorax 6: 137, 1951.
10. Wright, D.: The Blood Supply of Abnormal Tissues in the Lungs, J. Path. & Bact. 47: 489, 1938.
11. Marchand, P., Gilroy, J. D., and Wilson, V. H.: An Anatomical Study of the Bronchial Vascular System and Its Variations in Disease, Thorax 5: 207, 1950.
12. Cudcowicz, L., and Armstrong, J. B.: The Bronchial Arteries in Pulmonary Emphysema, Thorax 8: 46, 1953.
13. Miller, W. S.: The Lung, Springfield, Ill., 1950, Charles C Thomas, publisher.
14. Berry, J. L., and de Burgh Daly, I.: The Relation Between the Pulmonary and Bronchial Vascular Systems, Proc. Roy. Soc., s B, London 109: 319, 1931.
15. Ghoreyeb, A. A., and Karsner, M. T.: A Study of the Relation of Pulmonary and Bronchial Circulation, J. Exper. Med. 18: 500, 1913.
16. Verloop, M. C.: The Arteriae Bronchiales and Their Anastomoses With the Arteria Pulmonalis in the Human Lung: A Microanatomical Study, Acta anat. 5: 171, 1948.
17. Gray, F. D., Lurie, P. R., and Whittemore, R.: Circulatory Changes in Chronic Pulmonary Disease, Yale J. Biol. & Med. 23: 380, 1951.
18. Steinberg, I., and Robb, G. P.: Mediastinal and Hilar Angiography in Pulmonary Disease, Am. Rev. Tuberc. 38: 557, 1938.
19. Spatt, S. D., and Grayzel, D. M.: Cor Pulmonale, Am. J. Med. 5: 252, 1948.

20. Kountz, W. B., Alexander, M. L., and Prinzmetal, M.: The Heart in Emphysema, Am. Heart J. 11: 163, 1936.
21. Scott, R. W., and Garvin, C. F.: Cor Pulmonale: Observations in Fifty Autopsy Cases, Am. Heart J. 22: 56, 1941.
22. Spain, D. M., and Handler, B. J.: Chronic Cor Pulmonale, Arch. Int. Med. 77: 37, 1946.
23. Brofman, B. L., Charms, B. L., Kohn, P. M., Elder, J., and Rizika, M.: Unilateral Pulmonary Artery Occlusion in Man, J. THORACIC SURG. 34: 206, 1957.
24. Nemir, P., Stone, H. H., Hawthorne, H. R., and Mackrell, T. N.: Further Experiences With the Method of Controlled Unilateral Pulmonary Artery Occlusion in the Study of Lung Function, J. THORACIC SURG. 32: 563, 1956.
25. Creech, O., Krementz, E. T., Ryan, R. F., and Winblad, J. N.: Chemotherapy of Cancer, Ann. Surg. 148: 616, 1958.
26. Hamilton, W. F., Moore, J. W., Kinsman, J. M., and Spurling, R. G.: Studies on the Circulation. IV., Am. J. Physiol. 99: 534, 1932.
27. Spencer, W. A., Thistlethwaite, T. R., and Albert, S. N.: A Simplified Method for Blood Volume Determination Using Radioactive Isotopes, S. Forum 7: 3, 1956.

(For Discussion, see page 699)

AN EXPERIMENTAL STUDY OF PULMONARY ARTERY REPLACEMENT

Joseph W. Gilbert, M.D. (by invitation), William P. Cornell, M.D. (by invitation), and Theodore Cooper, M.D., Ph.D. (by invitation), Bethesda, Md.

THE CORRECTION of certain congenital cardiovascular malformations, such as atresia of the main pulmonary artery, varieties of persistent truncus arteriosus, and transposition of the great vessels, is contingent upon effecting communication between the right ventricle and the pulmonary arterial tree. Replacement of the bifurcation of the pulmonary artery distal to the valve with an aortic homograft was undertaken by Robinson and his associates[1] in exploring means for treating thrombosis of the pulmonary arteries. They concluded that this technique was unsatisfactory since degeneration of the grafts was evident as early as 70 days postoperatively. Donovan and his co-workers[2] employed venous-lined tubes of polyethylene or homologous trachea between the right ventricle and the left pulmonary artery; the lumens usually became obstructed within 3 or 4 weeks. The technical problems and the hemodynamic consequences attending insertion of valveless Edwards-Tapp Teflon prostheses between the right ventricle and a main branch of the pulmonary artery comprise the subject of this study.

METHOD

Adult mongrel dogs, weighing 13 to 17 kilograms, were anesthetized with thiopental sodium (30 mg. per kilogram) and the lungs were mechanically ventilated through a cuffed intratracheal tube with 100 per cent oxygen. Digoxin, 0.015 mg. per kilogram to 0.03 mg. per kilogram, was administered intravenously following induction of anesthesia and the left or right thorax was entered through the fourth intercostal space (Fig. 1). Pressures in the femoral artery, right ventricle, and a subsegmental tributary of the ipsilateral pulmonary artery were measured by means of Statham transducers and inscribed, with Lead II of the electrocardiogram, on a multichannel recorder. The right or left pulmonary artery was mobilized and divided and an Edwards Tapp prosthesis of woven Teflon, $\frac{5}{16}$ to $\frac{3}{8}$ inch in diameter and 6 to 8 cm. in length, was approximated to its distal end by means of a continuous 5-0 arterial suture. The proximal end, supported by an inclosed extraluminal polyethylene sleeve, was inserted into the outflow tract of the right ventricle through a purse string suture during 30 to 60 seconds of caval occlusion. The prosthesis was fixed to the myocardium by means of additional interrupted sutures. The thorax was closed anatomically.

From the Clinic of Surgery, National Heart Institute, Bethesda 14, Md.

Read at the Fortieth Annual Meeting of The American Association for Thoracic Surgery at Miami Beach, Fla., May 11-13, 1960.

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Right heart catheterization and angiocardiography were carried out in all survivors 3 to 90 days after operation. Serial radiographs (2 per second) were made following the selective right ventricular injection of 70 per cent Urokon (1 c.c./Kg.). In all animals in which initial patency of the prosthesis was demonstrated, the study was repeated after an interval of at least 90 days (Fig. 2). Dogs in which the grafts were shown to be obstructed were sacrificed and the causes of failure determined. Three animals having patent grafts were sacrificed at intervals of 5 days to 171 days to observe the lumens, anastomoses, and ventricular orifices of the prostheses.

RESULTS

Fifteen of the 25 dogs in which the procedure was performed survived. Two died during operations because of technical errors. Delayed hemorrhage from ventricular detachment of the prosthesis (2 dogs) and disruption of the pulmonary artery anastomosis (1 dog) accounted for 3 deaths. Massive postoperative atelectasis resulted in the loss of 3 dogs and infection caused the death of 2. In 1 animal, which died with multiple pulmonary abscesses, the prosthesis was obstructed at the pulmonary artery suture line by thrombus. The grafts were patent in the 4 remaining dogs in which death could not be ascribed to technical inadequacy.

The acute circulatory changes associated with insertion of the valveless unilateral prosthesis are illustrated in Fig. 3. Moderate elevation of systolic pressure and slight elevation of end-diastolic pressure occurred in the right ventricle. The pulse pressure was increased in the pulmonary artery distal to the graft, the cardiac rate was increased, and the systemic arterial pressure remained at control level.

Patency of the prosthesis was demonstrated in 10 of the 15 survivors at the time of the first study, 3 to 90 days postoperatively. The causes of early obstruction were kinking because of excessive graft length or atelectasis in three instances, improper ventricular insertion in one, and infection in one. Four prostheses which were initially patent were found to be obstructed at 3 months. In three, improper right ventricular insertion was responsible for obstruction, and in one, infection.

The lumens of patent grafts were lined by thin fibrinous films at 5 days, and by 170 days this had become a densely adherent gray membrane. Neither the suture lines nor the ventricular orifices showed evidence of stenosis (Fig. 4).

TABLE I. POSTOPERATIVE RIGHT HEART CATHETERIZATION DATA

DOG NO.	POSTOP. INTERVAL (DAYS)	F.A. (MM. Hg)	R.A. (MM. Hg)	R.V. (MM. Hg)	P.A. S/D, MEAN (MM. Hg)	HEART RATE
472	3	160/100	3-9	32/5		148
502	6	140/100	4-8	36/6		140
582	19	172/122	3-7	40/6		164
	90	164/110	4-9	38/5		160
975	49	135/94	3-6	36/5		142
	90	193/147	4-9	35/5	28/6, 14	180
832	90	186/102	4-7	38/8		140
Anesthetized normal		150/100		26/6		130

Legend: F.A. = femoral artery. R.A. = right atrium. R.V. = right ventricle. P.A. = pulmonary artery (contralateral).

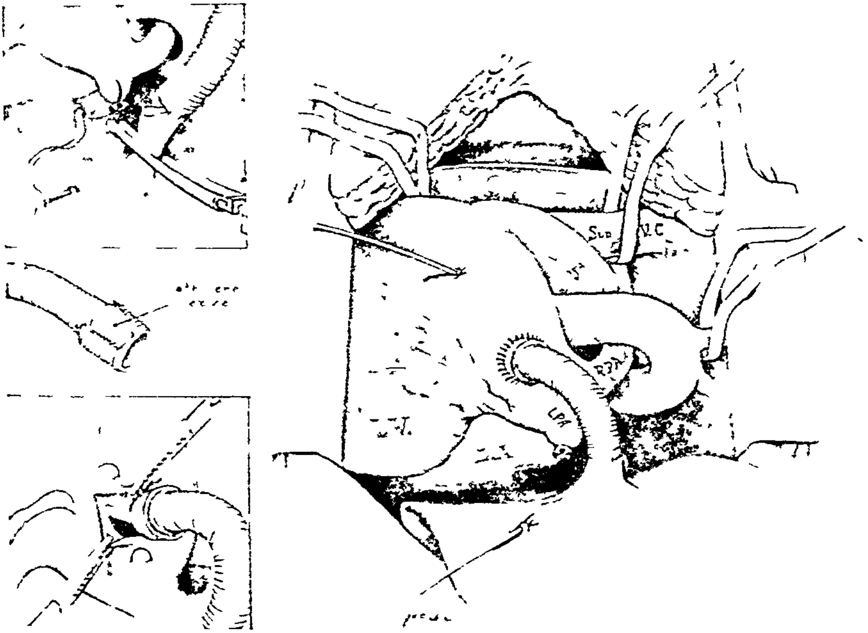

Fig. 1.—Method employed in replacement of the left main pulmonary artery with woven Teflon graft. The proximal end of the prosthesis is inserted into the right ventricle during brief caval occlusion.

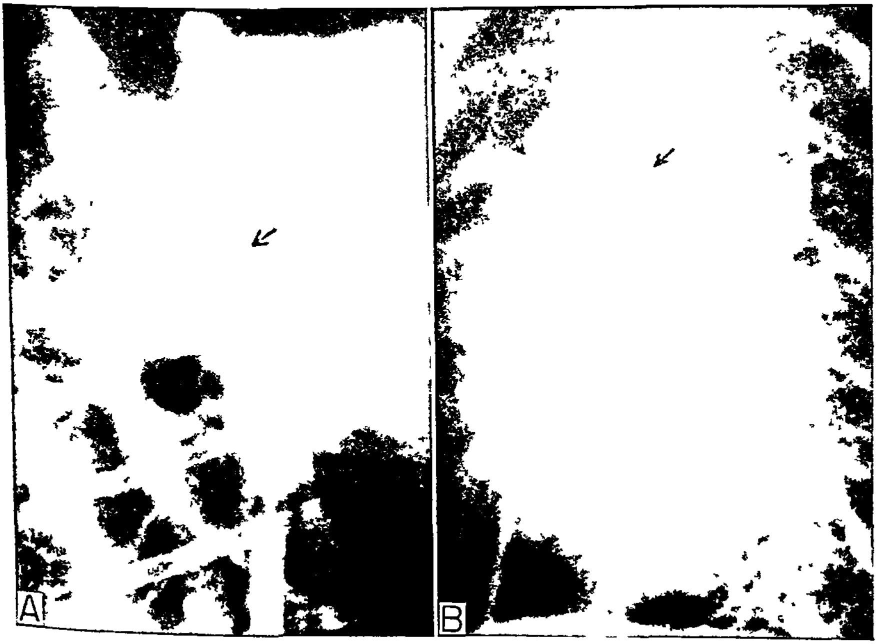

Fig. 2.—Angiocardiogram showing patent prosthesis between right ventricle and right pulmonary artery (*A*) in lateral view at 19 days and (*B*) in anteroposterior view at 90 days.

Postoperative right heart catheterization data comprise Table I. Minimal elevation was seen in the systolic pressure in the right ventricle; the systolic and diastolic pressures in the opposite pulmonary artery were normal. Systemic arterial hypertension and tachycardia of moderate degree were present in all animals, which were under light thiopental sodium anesthesia.

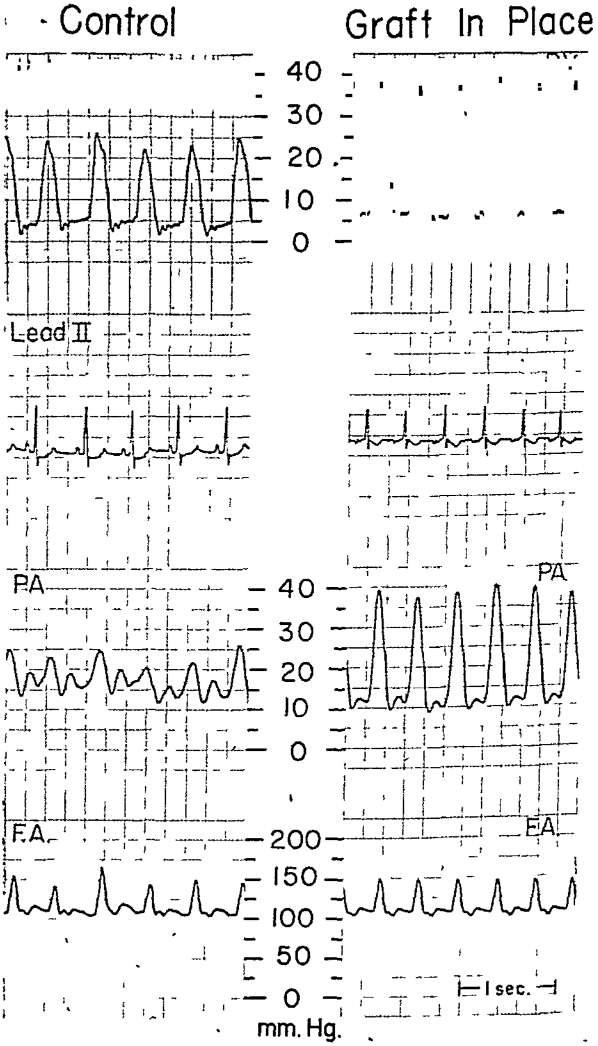

Fig. 3.—Acute circulatory changes associated with the insertion of a valveless graft between the right ventricle and the left pulmonary artery. *R.V.* = right ventricle; *P.A.* = pulmonary artery; *F.A.* = femoral artery.

COMMENT

The replacement of portions of the main pulmonary arterial tree by means of Edwards-Tapp Teflon prosthesis seems feasible. Although the use of such material for this purpose appears to afford certain advantages over venous or aortic homografts, proper evaluation of its ultimate fate in the lesser circulation requires more prolonged observation. Unlike grafts inserted in systemic vessels, pulmonary artery replacements must traverse the mediastinum virtually unsupported by adjoining structures. This, together with the low pressure in the pulmonary artery, predisposes toward obstruction by kinking, especially in the event of atelectasis. Despite the relative sparsity of adjacent tissues, intraluminal healing of the Teflon prostheses appears to progress in accordance with the process described[3] following their insertion in systemic arteries. Stricture at the site of anastomosis, which has been reported after synthetic graft replacement of segments of the inferior vena cava,[4-7] has not been observed in this experience. No histologic changes have been discernible in the vessels or parenchyma of the lung distal to the valveless grafts.

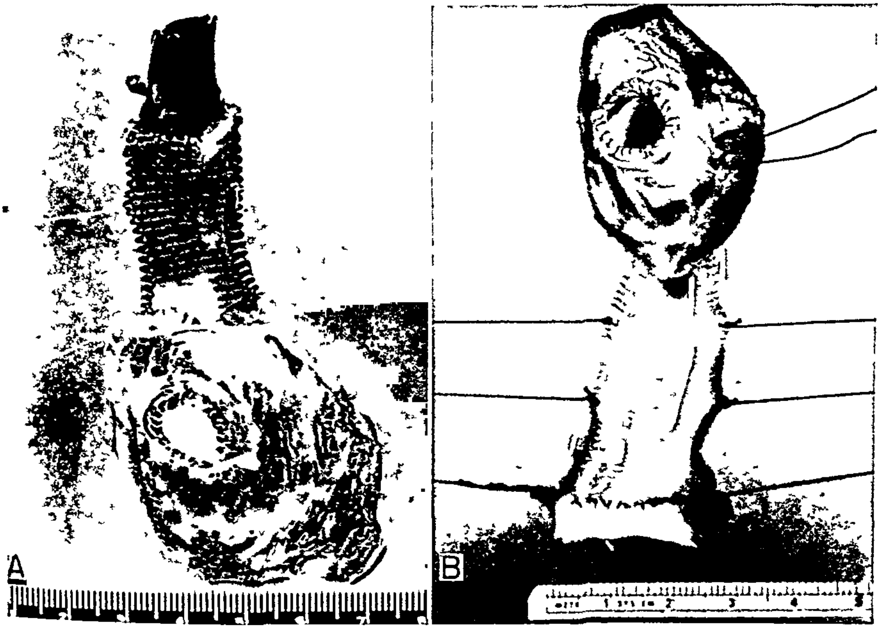

Fig. 4—Teflon prostheses from dogs sacrificed *(A)* at 5 days and *(B)* at 171 days following insertion

Pressure measurements in the right ventricle demonstrate small but significant changes in systolic and end-diastolic pressures following insertion of a valveless unilateral pulmonary artery prosthesis and dilatation of this cardiac chamber was regularly noted. These findings reflect the increased end-diastolic volume and stroke output caused by regurgitation from one lung. The use of a graft of excessive length increases the resistance to flow to the respective lung, resulting in further elevation of right ventricular pressure. Increasing the flow through the prosthesis by occluding the opposite pulmonary artery accentuates this gradient and the elevations in systolic and end-diastolic pressures in the right ventricle. These observations emphasize the critical factors of graft length and proportion which must be considered in replacement of the main pulmonary artery and its bifurcation. Although the infliction of regurgitation in the performance of pulmonary valvulotomy has not generally been accorded serious concern, Fowler and Duchesne[8] have shown experimentally that the lesion may not be entirely innocuous. Replacement of the pulmonary artery with a graft which is inelastic, as well as valveless, imposes a more marked burden upon the right ventricle. The availability of a satisfactory prosthetic valve will significantly simplify this problem. Finally, it must also be recognized that the individual variables which may affect the hemodynamic consequences of pulmonary artery replacement in a patient with congenital heart disease may not necessarily be anticipated from studies performed in the normal dog.

SUMMARY

Woven Edwards-Tapp Teflon blood vessel prostheses were inserted between the right ventricle and a main branch of the pulmonary artery in 25 dogs, 15 of which survived chronically. Right heart catheterization and selective angiocardiography were performed in the survivors and in 10 the grafts were found *to be patent 5 days to 90 days postoperatively. Repeat studies disclosed* that in 4 animals, in which the grafts were initially patent, obstruction subsequently occurred within 90 days. The causes of failure, certain pathologic findings, and hemodynamic observations pertinent to this use of vascular prostheses are considered.

REFERENCES

1. Robinson, G., Glotzer, P., Gilbert, M., and Hurwitt, E. S.: Aortic Homograft Replacement of the Main Pulmonary Artery, J. THORACIC SURG. 36: 555, 1958.
2. Donovan, T. J., Hufnagel, C. A., and Eastcott, H. H. G.: Techniques of Endocardial Anastomosis for Circumventing the Pulmonic Valve, J. THORACIC SURG. 23: 348, 1952.
3. Edwards, W. S., Boyles, P., Forrest, C., and Waibel, P.: Progress in Synthetic Graft Development. An Improved Crimped Graft of Teflon, Surgery 45: 298, 1959.
4. Deterling, R. A., and Bhonslay, S.: Use of Vessel Grafts and Prostheses for Relief of Superior Vena Caval Obstruction, Surgery 38: 1008, 1955.
5. Ohara, I., and Sakai, T.: Transplantation of the Large Venous System With Various Blood Vessel Substitutes, Surgery 42: 928, 1957.
6. MacLean, L. D., Phibbs, C. M., Flom, R. S., and Brainard, J. B.: Replacement of Vital Veins: An Experimental Study, Ann. Surg. 149: 549, 1959.
7. Sauvage, L. R., and Wesolowski, S. A.: Anastomoses and Grafts in the Venous System With Special Reference to Growth Changes, Surgery 37: 714, 1955.
8. Fowler, N. O., and Duchesne, E. R.: Effect of Experimental Pulmonary Valvular Insufficiency on the Circulation, J. THORACIC SURG. 35: 643, 1958.

(For Discussion, see page 699)

A SIMPLE STAPLING DEVICE FOR THE ANASTOMOSIS OF BLOOD VESSELS

Timothy Takaro, M.D., Oteen, N. C.

A NUMBER of instruments have recently been described for the anastomosis of blood vessels by means of the simultaneous application of multiple small staples circumferentially.[1-5] While the usefulness of such devices, either experimentally or clinically, has not yet been established, there is certainly room for the opinion that instruments which can perform a technically perfect anastomosis speedily at every application may ultimately find utility, especially in small blood vessel anastomoses and in organ transplantation. Therefore, basic experimental studies of the use of such instruments seem to be indicated.

A device of but few components and of simple design has been constructed which has made possible the mechanical anastomosis of prosthetic grafts to blood vessels by intubation of the blood vessel, the stapling being carried out while blood is flowing through the junction between the vessel and the graft. This instrument, the technique used, and the results of laboratory experiments with this technique are described below.

DESCRIPTION OF DEVICE

One jaw of a previously described cylindrical vessel coupling device,[6, 7] bivalved to permit removal, was modified by fitting it with eight tiny shafts for housing staples and for guiding two four-pronged staple drivers (Figs. 1 and 2). On the opposing jaw, eight, precisely placed, specially shaped indentations for clinching the staples were fashioned. A circular bivalved nut which was fitted onto the staple-housing unit served to force the staple driver prongs into the shafts, thereby pressing eight tiny staples across the interval between the clincher unit and the staple-housing unit, and causing the legs of the staples to be bent inward toward each other. The staples were made by hand of surgical stainless steel wire, or dental gold clasp wire, of 0.012 in. diameter, cut to produce a sharp point on each leg (Fig. 3). Leg lengths of the staples varied from 0.074 to 0.125 in. The width of the staples at the base was 0.086 in. The internal diameter of the staple-housing unit was 9 mm. and the external diameter, 12 mm.

METHOD

Elasticized Dacron grafts* were interposed in the thoracic aorta of 25 normothermic dogs, weighing 13 to 25 kilograms, using the stapling device just described for effecting one

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*"Fluflon" Dacron, manufactured by the Bentley, Harris Manufacturing Company, Conshohocken, Pa. Two different sizes were used, measuring 13 mm. and 17 mm. flat.

anastomosis (Fig. 4). The other was sutured with arterial silk, with the aid of a previously described coupling device.[7] The staple housing unit was first loaded with eight staples Next, the two four-pronged staple drivers were engaged in the staple housing shafts Then one end of an elasticized Dacron prosthesis was passed through the lumen of the staple housing unit and cuffed back upon it, covering the openings of the staple housing shafts The other end of the graft was cuffed back upon the graft-bearing portion of the other coupling device. The prosthesis was preclotted with fresh blood.

The animals were anesthetized with Nembutal and the trachea was intubated. A positive pressure respirator was attached. The left pleural cavity was entered through the fifth

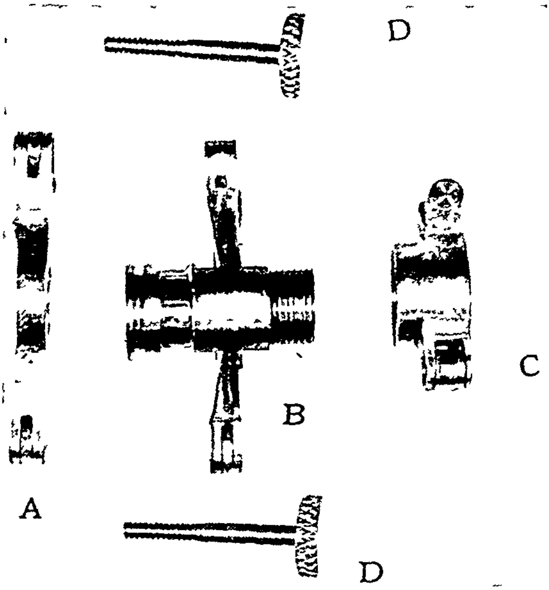

Fig 1 —Stapling device disassembled, side view.

A, Clincher unit, hinged to allow removal

B, Staple-housing unit, with staple drivers in place This unit is also hinged Note shallow groove near clincher end

C, Staple-driving nut, hinged to permit removal

D, Bolts to approximate clincher and staple-housing units

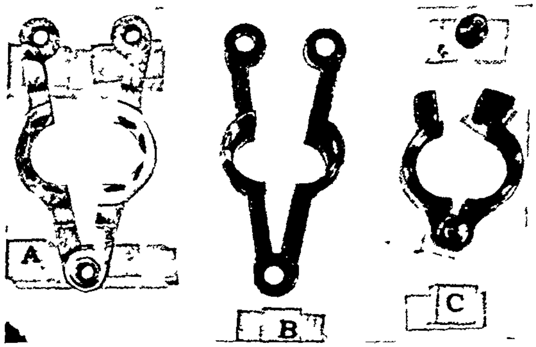

Fig 2 —Stapling device, disassembled, end-on view.

A, Clincher unit with jaws opened showing four depressions engraved in each semicircular jaw to clinch staples

B, Staple-housing unit with jaws opened showing four staple-housing shafts positioned exactly opposite the engraved depressions on the clincher unit jaws Staple drivers and staples have been removed

C, Circular staple-driving nut opened with fastening bolt removed and shown above the nut

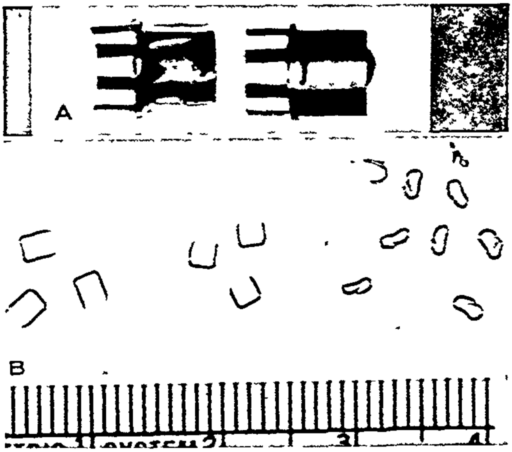

Fig 3 —*A*, Close-up of the 2 semi-circular staple drivers, the four prongs of which fit exactly into the four staple-housing shafts of each jaw of staple-housing unit.

B, Close-up of staples At *left*, long-legged staples, in *middle*, short-legged staples (see text); at *right*, staples which have been recovered from an aortic graft anastomosis, by digesting away the tissues, to show shape of clinched staples One at top was improperly deformed.

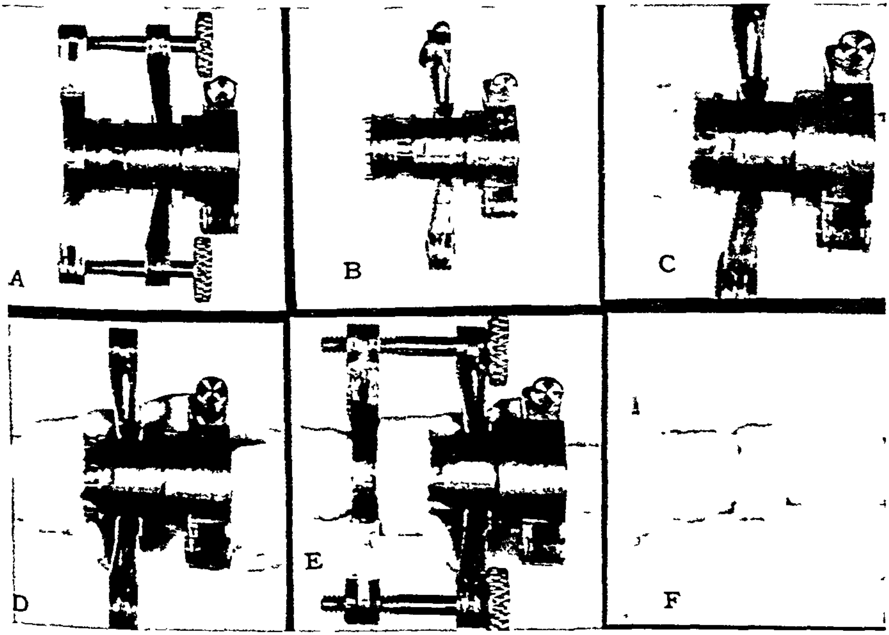

Fig 4 —Steps in technique of stapling prosthesis to aorta

A, Assembled stapler, side view

B, Stapler partially disassembled. Staple-housing unit loaded with staples, the points of which are just visible, protruding from staple shafts for demonstration only In use, they are retracted within the shafts, out of sight. Note staple drivers in place

C, Dacron graft pulled through loaded staple-housing unit and cuffed back upon the groove overlying staple shafts

D, Everted graft inserted into aortic lumen It is held in place temporarily by a wire loop held in a tonsil snare (not shown), until bolts can be applied Ordinarily, clincher unit (also not shown) has already been positioned around the intact aorta.

E, Bolts passed through staple-housing unit arms have engaged clincher unit arms and approximated the jaws of the stapler, locking aorta and graft in the interval between the jaws The circular staple-driving nut has been applied and tightened against the staple drivers, forcing the eight staples across the interval between the jaws of the stapler and clinching them, completing the mechanical anastomosis

F, The stapler has been removed by disengaging the two main bolts, as well as the bolt fastening the circular nut, and opening the 3 major components on their hinges. This shows the appearance of the anastomosis after trimming off excess aorta.

interspace; the mediastinal pleura was incised and reflected back from the aorta. The first five pairs of intercostal arteries were divided between ligatures, mobilizing the proximal descending thoracic aorta. The appropriate semi-circular opposing jaws of each coupling device were placed about the intact aorta near the proximal and distal ends of the isolated segment and the matching pairs fastened together to complete the circle. A holding suture of 5-0 arterial silk was placed near the proximal and distal ends of the isolated, intact aorta, and two loops of braided wire were placed around the aorta and tied onto tonsil snares, which were held ready for tightening. The aorta was then cross-clamped just distal to the subclavian artery and also at the level of the sixth intercostal artery, and the segment of aorta between the clamps was incised longitudinally.

The staple-housing unit bearing the everted Dacron prosthesis was inserted into the lumen of the aorta at one end of the isolated segment, through the incision in the aortic wall. In order to keep the device from slipping out again while the approximating bolts were being applied, the device was held firmly in place in the aortic lumen by tightening the wire loop around that portion of the aorta which hugged the everted cuff of prosthesis. The two bolts were then slipped through the holes in the arms of the staple-housing unit, engaged in the holes in the arms of the opposing staple-clinching unit, and tightened a determinate distance, sufficient to close the gap between the two circular jaws of the stapling device and to lock the aorta and the graft together in the interval between the jaws, but not sufficient to allow crushing of the aortic wall.

A similar procedure was carried out at the other end of the isolated segment of aorta. Aortic continuity was thus restored by an indwelling Dacron prosthesis which was locked into place proximally and distally by coupling devices. The aortic occluding clamps were removed, restoring blood flow through the thoracic aorta. The wire loops were loosened and removed. The segment of incised aorta between the two coupling devices was resected.

The circular staple-driving nut was applied to the staple-housing unit and fastened in place with a small bolt. This circular nut was then turned clockwise on the unit, pushing the two staple drivers ahead, and forcing the eight small staples simultaneously through the graft and aortic walls and on into the indentations in the clincher unit. Further tightening of the nut with the aid of strong forceps caused the staples to be "clinched," that is, the staple legs were bent inward toward each other. This completed the mechanical anastomosis. The bolts approximating the 2 circular jaws were removed and the bivalved circular jaws of the stapler were opened and also removed. Bleeding between the staples was controlled by wrapping the anastomosis in gauze and applying moderate pressure. Occasionally a few sutures of silk or a second row of staples had to be applied to control bleeding. The distal anastomosis was sutured with 5-0 arterial silk in the usual manner, after which this vessel couple was also removed, leaving the stapled and sutured prosthesis in the mediastinum. Following closure of the mediastinum over the graft, the chest was closed and drained for a few hours by a negative pressure suction pump. Occasionally a blood transfusion was given during surgery. Antibiotics were sometimes used.

In 6 animals, for the reason just noted, two rows of staples, staggered with respect to each other, were placed. In 20 animals, the stapled anastomosis was the proximal one, while in 5, it was the distal anastomosis. Upon sacrifice or death of the animal, an autopsy was done and the engrafted aorta was recovered, opened, inspected, and photographed. Sections were taken across each anastomosis for histologic examination, after removal of the staples by fine wire cutters. The sutured anastomosis served as the control. From some animals, sections of both the stapled and sutured anastomoses, 1 cm. in width, were prepared and subjected to tensile strength measurements, using the inclined plane Scott tester,* the breaking point of the anastomosis being used as the end point. In 8 animals, thoracic aortography was performed at varying intervals following surgery.

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*Made available through the courtesy of the American Enka Corporation, Enka, N. C.

RESULTS

The procedure was carried out in 25 animals. The average time of aortic occlusion needed to interpose the graft and to lock it into place, re-establishing blood flow, was 5½ minutes. Aortas, ranging in diameter from 1.3 to 2.0 cm. in the blood-filled state, were successfully stapled with the single model available. There were two immediate failures, one of which resulted in death of the animal on the table. Five animals died at intervals of 1 day to 4 months after surgery of hemorrhage, infection, or pneumonia. In 2 of these, the graft was occluded. The remaining animals, including 3 which developed paralysis of the hindquarters, were sacrificed at intervals from 1 week to 8 months or were allowed to survive, 8 being kept for long-term study (see Table I). Of the 25 instances, the graft was patent in all but 2 as shown at autopsy, upon aortography or by palpation of femoral pulses. Aortograms showed varying degrees of narrowing at both anastomoses, ranging from slight to marked, depending upon the disparity between the diameter of the blood-filled aorta and the diameter of the graft (Fig. 5). Calculation of the area of the aortic lumen, proximal to the stapled anastomosis and at the anastomosis, showed a reduction in area up to 75 per cent in a few instances, although the area at the anastomosis averaged only 30 per cent less than the area of the lumen of the graft itself.

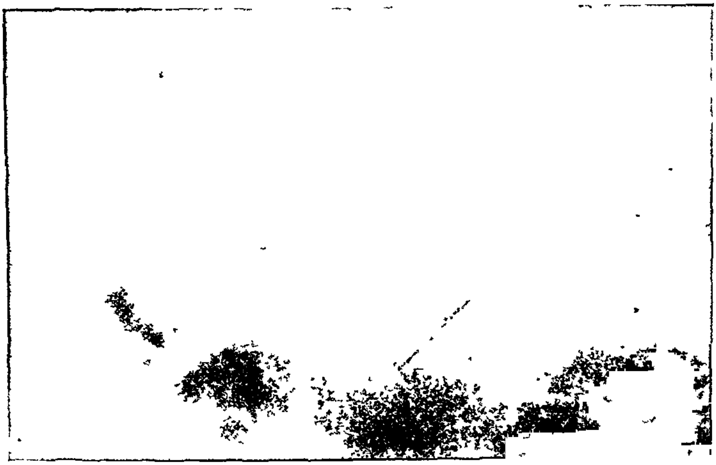

Fig. 5.—Thoracic aortogram, Animal 17, showing Dacron graft interposed in upper descending thoracic aorta. The proximal anastomosis, indicated by slight narrowing, was made with silk sutures with the aid of an Oteen vessel coupling device. The distal anastomosis was accomplished by the use of the stapling device and is indicated by the arrow.

The results of thirty-one tests of the breaking point of the anastomoses performed on the inclined plane tester favored the silk sutured anastomoses. This was true of the specimens from 3 animals sacrificed within 2 weeks of operation, as well as from 5 animals allowed to survive up to 8 months. The average breaking point of stapled anastomoses occurred at 2.6 pounds of stretch (range 1.2 to 5.2) compared with an average of 3.3 for silk (range 1.0 to 6.1).

TABLE I

NUMBER IN SERIES	NUMBER OF ROWS OF STAPLES AND SITE OF STAPLED ANASTOMOSIS	TIME OF AORTIC OCCLUSION (MINUTES)	BLEEDING FROM STAPLED ANASTOMOSIS	DURATION OF SURVIVAL (DAYS)	FATE OF ANIMAL	REMARKS
1	1 row Proximal	6	Minimal	120	Died	Graft thrombosed; micro abscesses around proximal anastomosis
2	1 row Proximal	8	Excessive	90	Sacrificed	Graft patent; small patch of fibrin deposit, distal portion of graft
3	1 row Proximal	5	Excessive	270	Alive	Animal in good health
4	1 row Proximal	7½	—	—	Technical failure	Clincher put on backward; operation changed; animal lost to this study
5	1 row Proximal	4½	Minimal	250	Sacrificed	Graft patent with smooth glistening lining of compact fibrous tissue
6	1 row Proximal	4½ + 24*	Excessive	8	Sacrificed	New batch of staples, too stiff to clinch; prolonged occlusion to reload stapler resulted in paralysis of hind limbs
7	1 row Proximal	4	Excessive	—	Died at operation	Technical failure: prosthesis too thick, staples too short to clinch; hemorrhage on table
8	1 row Proximal	5½	Minimal	105	Sacrificed	Graft patent; thick deposits of fibrin, distal ⅔ of graft
9	1 row Proximal	5½	Excessive	60	Died	Graft thrombosed; gross infection with abscess formation rupturing into esophagus
10	1 row Proximal	4	Excessive	21	Died	Graft patent; animal died of pneumonia
11	1 row Distal	5½	Moderate	30	Died	Graft patent; cause of death unknown; minimal inflammatory reaction
12	2 rows Proximal	6	Moderate	225	Alive	Animal in good health; moderate narrowing of anastomoses on aortogram
13	2 rows Proximal	5½	Moderate	221	Alive	Animal in good health; moderate narrowing of anastomoses on aortogram

14	2 rows Proximal	4	Minimal	180	Sacrificed	Graft patent; thick deposits of fibrin, middle half of graft
15	2 rows Proximal	8	Excessive	214	Alive	Animal in good health
16	2 rows Distal	5	Excessive	3	Sacrificed	Became paralyzed 3 days postop.; thrombus at pocketed distal anastomosis led to probable aortic embolus; graft patent
17	1 row Distal	7½	Excessive	120	Alive	Animal in good health
18	1 row Distal	4½	Excessive	80	Sacrificed	Graft patent; smooth thin lining; gross infection with abscess formation rupturing into esophagus
19	1 row Proximal	4½	Moderate	102	Alive	Animal in good health
20	2 rows Distal	3½	Moderate	98	Alive	Animal in good health
21	1 row Proximal	6	Excessive	45	Alive	Animal in good health
22	1 row Proximal	10 + 10*	Excessive	35	Sacrificed	Longitudinal tear in aorta required prolonged occlusion to suture; animal paralyzed in hindquarters postop. but began to recover; graft patent
23	1 row Proximal	3½	Moderate	14	Sacrificed	Graft patent
24	1 row Proximal	4	Excessive	1	Died	Died of massive hemorrhage between staples 1 day postop.; graft patent, anastomoses intact
25	1 row Proximal	5	Excessive	5	Sacrificed	Graft patent

*A second period of occlusion was necessary to reload stapler or to control hemorrhage.

PATHOLOGY

Grossly, there was a rather obvious ridge at the stapled anastomosis within the aortic lumen in most specimens, where the graft was cuffed back upon itself. This resulted in moderate narrowing of the lumen. Fibrin collected at the base of the ridge early; later, fibrous tissue bridged the gap between the aortic intima and the inner surface of the graft. This was usually not as well developed or as smooth as the union between the graft and the aorta at the sutured anastomosis. There was also a less obvious ridge and less narrowing of the lumen at the sutured anastomosis. There was little or no inflammatory reaction in the tissues surrounding the holes which remained after removal of the staples. The elastic fibers were compressed at the site of the staples, but not in the areas between staples. Occasionally there was disruption of elastic fibers at the anastomotic site, probably from excessive compression of the media by the stapling device. In contrast to the stapled anastomosis, there was usually a mild to moderate inflammatory reaction around the silk threads at the sutured anastomosis. Compression and, less commonly, disruption of elastic fibers, presumably due to the coupling device, were seen at this anastomosis also.

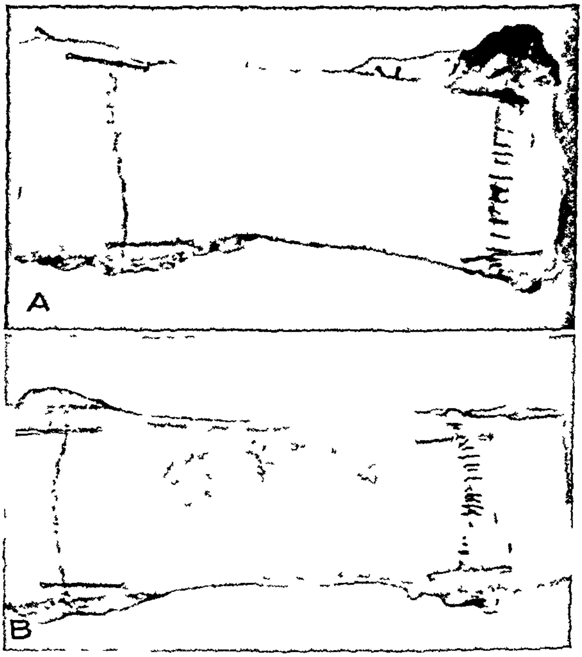

Fig. 6.—Gross specimens of stapled aortic Dacron grafts

A, Graft from animal sacrificed 8 months after operation; the staples are scarcely visible and are covered with thin smooth fibrous tissue as is the sutured anastomosis at the other end of the graft

B, Graft from animal sacrificed 6 months after operation which shows deposits of fibrin, several millimeters in thickness, in mid-portion of graft.

The grafts were lined in the immediate postoperative period with fibrin, which later became organized into a compact layer of fibrous tissue, grossly smooth and glistening (Fig. 6). However, in several specimens, deposits of fibrin, up to a few millimeters in thickness, were found in the mid-portions of the graft as late as 6 months following operation. Two grafts were completely thrombosed in their mid-portions, 2 and 4 months following operation. In these animals there was microscopic or gross evidence of infection.

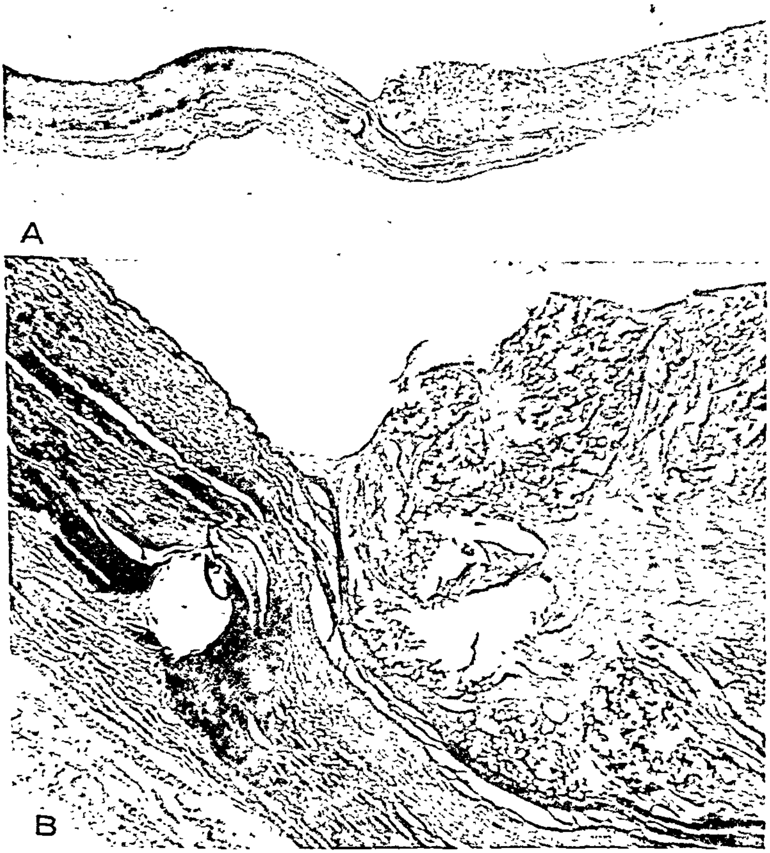

Fig. 7.—Microscopic section of stapled aorta-Dacron anastomosis.

A, Specimen shows everted cuff of graft (*right*) within lumen of aorta. Note ridge formed by cuff of graft. The surface facing the lumen of the aorta is at the top. (Elastic tissue stain; ×4.5.)

B, Close-up of same specimen. Compression of elastic fibers by staple is well seen. There is no inflammatory reaction and no other medial injury. (Elastic tissue stain; ×30.)

DISCUSSION

The earliest report of a vascular stapling apparatus, by Gudov, 10 years ago, is in Russian and was not available to us. This is apparently the precursor of the device described more recently by Androsov,[1] which employs tantalum wire staples and is a complex, precision instrument of approximately 26 parts. It is said to be usable for suturing vessels from 1.3 to 15 mm. in diameter. Eversion of the ends of both vessels being joined is required. The instrument was reported to have been tested in 394 experimental operations on dogs with excellent results; there was no narrowing at the anastomotic site, no thrombosis, no scar formation, and no inflammatory reaction around the clips. Details of these experiments were not given.

A Hungarian stapling apparatus was described in 1953 by Bikfalvi and Dubecz[2] along with details of its use in 47 animals. Stapling of the abdominal aorta with this device was successfully accomplished in 27 animals, of which there were 18 survivors. The details of construction of the device are not easy to make out. Suturing was accomplished by U-shaped silver clamps.

The third report of a blood vessel stapler to appear was that of Vogelfanger and Beattie from Canada.[3] Again, the finer details of the mechanics of the instrument are not clear, but the construction seems to be considerably simpler than that of the preceding two. Tantalum U-shaped staples were used in the abdominal aorta of 10 pigs. Few details of the experimental work done were given in this report.

The description of a stapling device of Japanese construction, by Inokuchi, next appeared.[4] This resembles the Russian stapler but is of simpler design. Alloyed steel clips were used in numerous animal experiments. Again, few details were reported. However, in a personal communication, Dr. Inokuchi[8] kindly sent details of the results of experiments in 68 animals, comparing suturing techniques with stapling techniques in vessels ranging from 2.6 mm. to 9.0 mm. in size. There was clear-cut superiority of the stapling technique over suturing by hand using the Carrel technique, in both veins and arteries.

The fifth stapling device of which we have knowledge is of a totally different design and was reported by Sterling of Philadelphia.[5] This instrument does not place all the staples into the anastomosis simultaneously as the others do, but instead, singly, by a device which rotates the anastomosis through the stapler. No experimental or clinical applications were described.

Our instrument, the sixth to appear, has the virtue of simplicity of design since it consists of but eight parts. It has functioned successfully over a fairly broad range of vessel sizes. Staples have been made of both stainless steel and of a gold alloy.

The method of anastomosing graft to vessel by intubation of the vessel with the everted graft seems attractive because the vessel wall need not be traumatized by instruments nor everted on the coupling device. It seems to be considerably easier technically to intubate a vessel than it is to evert the cut end of a vessel over a device, especially if the vessel wall is thick or stiff because of disease. The technical excellence of some anastomoses, the metallic, nonreactive nature of the staples, and their minimal contact with the blood stream also recommend stapling methods generally. Speed of effecting the union is another advantage.

On the other hand, the need for a special device of the correct size, smaller than the vessel to be anastomosed, may prove to be a serious disadvantage when working with vessels of small caliber. The collections of fibrin in the mid-portion of some grafts may be taken as evidence of the effects of turbulence due to narrowing at the anastomotic junction in these animals. The thickness of the graft material (the everted cuff was 2 mm. in thickness) and the relative rigidity of the thick-walled thoracic aorta undoubtedly exaggerated the degree of narrowing which this technique produces. It is possible that with thin-walled veins as grafts to small arteries the degree of narrowing at the anastomosis may be insignificant. The report by Androsov and the experimental data provided by Inokuchi support this view. Our own experience with the use of this stapler in end-to-end anastomosis of the divided superior vena cava in animals also encourages us to expect better results with thin-walled vessels and prostheses.

Another disadvantage of this technique is the need for graft material of sufficient elasticity to prevent wrinkling when the graft is everted upon the stapler. Braided nylon, elasticized "Fluflon" Dacron, and homografts, as well as autografts, have all been used successfully in such devices.

Excessive bleeding between staples may be overcome by diminishing the distance between staples or by adding a second row of staples, staggered with respect to the first row.

Cuffing of the blood vessel over the graft makes it necessary to free up longer segments of blood vessel than the ordinary suturing techniques require. It is possible, however, that the advantages of obtaining technically excellent anastomoses in small vessels, or speedy anastomoses in large vessels with multiple branches (aortic arch, thoracoabdominal aorta), by mechanical means may outweigh the disadvantages of the additional dissection required to provide adequate cuffs of vessels.

SUMMARY AND CONCLUSIONS

1. A simple device, of but eight parts, for anastomosing a prosthetic graft to the canine thoracic aorta by intubating the aorta with the everted graft to achieve union is presented. Stapling is accomplished while blood is flowing through the device.

2. The instrument was used to interpose an elasticized Dacron graft in the descending thoracic aorta of 25 animals. There were 2 operative deaths, and 2 late deaths because of infection, with thrombosis of the graft. The remaining animals had patent grafts with anastomotic junctions which were technically excellent for the most part.

3. Significant narrowing at the anastomotic junction, which was due in part to disparity between the aorta and the graft and in part to cuffing of the vessel over the graft and of the graft upon itself, was observed in some animals. This may be overcome if prostheses sufficiently thin and elastic can be produced to allow temporary distortion by the stapling device, until stapling can take place. Vein grafts would probably answer the purpose.

4. A smaller model of the instrument, suitable for use in vessels 3 mm. in diameter, is being constructed. It is in the area of small vessel anastomoses that such devices may find their greatest usefulness.

We wish to acknowledge with gratitude the very real contribution of Mr. A. W. Chattaway of the Asheville Tool and Gauge Company in helping to plan this stapling device and in constructing the initial model.

REFERENCES

1. Androsov, P. I.: New Method of Surgical Treatment of Blood Vessel Lesions, A. M. A. Arch. Surg. 73: 902-910, 1956.
2. Bikfalvi, A., and Dubecz, S.: Observations in Animal Experiments With Mechanized Vessel Suture, J. internat. chir. 13: 481-496, 1953.
3. Vogelfanger, I. J., and Beattie, W. G.: A Concept of Automation in Vascular Surgery: A Preliminary Report on a Mechanical Instrument for Arterial Anastomosis, Canad. J. Surg. 1: 262-265, 1958.
4. Inokuchi, K.: A New Type of Vessel Suturing Apparatus, A. M. A. Arch. Surg. 77: 954-957, 1958.
5. Sterling, J. A.: Stapling Small Blood Vessels, J. Albert Einstein Med. Center 7: 192-193, 1959.
6. Takaro, T., and Grimes, T. P.: Reconstruction of the Thoracic Aorta With the Aid of a Vascular Coupling Device (Vessel Couple): Report of a Case, J. Thoracic Surg. 37: 93-99, 1959.
7. Takaro, T.: Experimental Replacement of Segments of the Upper Thoracic Aorta With the Aid of Vessel Couples, Am. J. Surg. 98: 617-622, 1959.
8. Inokuchi, K.: Personal communication, 1960.

(For Discussion, see page 699)

EXPERIMENTAL LEFT CORONARY ARTERY PERFUSION THROUGH AN AORTOTOMY DURING CARDIOPULMONARY BYPASS

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A DIRECT surgical approach on the aortic valve often necessitates a prolonged aortotomy, during which time the maintenance of myocardial nutrition is mandatory. The desirability of utilizing coronary artery perfusion to maintain nutrition in the bypassed heart with an ascending aortotomy is now well established. Clinically, we have found left coronary artery perfusion to be very satisfactory and the approach to the aortic valve is facilitated with a single cannula in the operative field.[1] The difficulties associated with retrograde coronary perfusion have been presented by Shumway[2] and Melrose.[3]

Our interest in experimental coronary artery perfusion began 2 years ago during the laboratory investigation of prosthetic aortic valve replacement. It was immediately apparent that the lack of a suitable cannula tip to accommodate the coronary ostia of the dog limited successful coronary artery perfusion through an open aortotomy. Other investigators have reported similar experiences.[2, 4] Fig. 1 shows several cannulas which were studied before the tip (Fig. 1, c) now used experimentally for left coronary artery perfusion was developed. The multiple holes present are necessary to avoid obstruction of the blood flow to early branches of the left coronary artery

EXPERIMENTAL METHOD

Sixty-one dogs (10.9 to 18 kilograms) were studied, 15 as controls, 24 in acute experiments, and 22 as survivor animals. Sodium pentobarbital anesthesia was used and positive endotracheal pressure (9 to 12 cm./water) was maintained by a mechanical respirator. A right thoracotomy through the fourth intercostal space and complete pump dependency (utilizing a disc oxygenator) were employed. The ascending aorta was cross-clamped within the pericardium and a 2 cm. oblique incision was made just above the aortic valve. The 15 control animals were studied by allowing blood from the left ventricle to flow freely through the open aortotomy, where it was removed by suction until either ventricular fibrillation or cardiac arrest occurred. In the remainder of the animals, a single coronary perfusion cannula, connected either to the arterial line of the pump or to a reservoir (500 ml. bottle)

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suspended 100 cm. to 110 cm. above the heart, was inserted into the left coronary ostium. Blood flow from the left ventricle was aspirated through the aortotomy. The right coronary ostium was not perfused. The suspended reservoir maintained a constant pressure of 74 to 80 mm. Hg[5] and continuous perfusion was performed for periods of 15 to 60 minutes at temperatures between 28° and 36° C. (esophageal and rectal). Coronary artery flow rates measured prior to perfusion varied from 50 ml. to 150 ml. per minute. A cannula was placed into the right auricle in 17 of the animals studied and total coronary venous flows (coronary sinus plus anterior cardiac venous return) were measured with a graduate cylinder; coronary venous samples for oxygen determination were drawn at intervals. Distal aortic pressures, continuous electrocardiographic tracings, coronary venous flows, temperatures, and coronary arteriovenous oxygen saturations (determined photoelectrically) were recorded. At the completion of coronary artery perfusion, the aortotomy was closed, the aortic clamp released, and pump dependency discontinued as soon as the animal's temperature reached 34° C. A section of Gelfoam saturated in protamine was placed over the aortotomy immediately after closure to produce local clotting until protamine sulfate had been administered systemically. Postoperative electrocardiograms were taken at intervals in the survivor animals. Digitalis was used in only 2 animals that died within a few hours after operation.

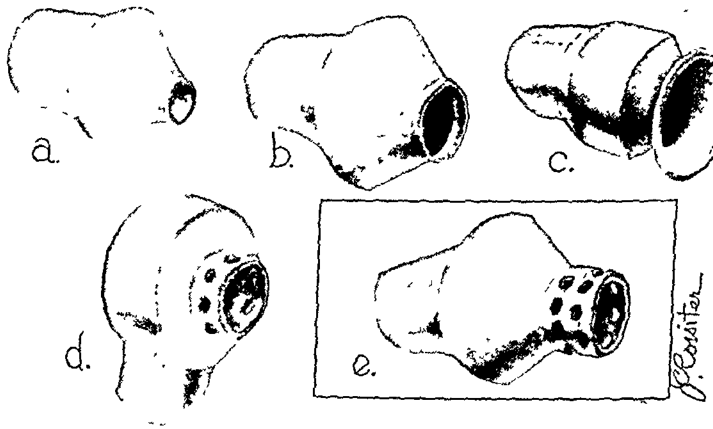

Fig. 1—These metal cannula tips were studied during this investigation in developing tip *e*, now in use for left coronary artery perfusion in the experimental animal. Tips *a*, and *c*, were designed to fit within the coronary ostium and did not have to be held in place. Tip *e*, may be used on either a malleable or firm metal cannula; it is 5 mm. in length with an internal diameter of 3.5 mm

RESULTS

The success of this investigation was limited by several factors, (1) the need for a specially designed cannula tip to accommodate the dog's left coronary ostium, (2) anatomic variations of the left coronary artery characterized by an immediate bifurcation, trifurcation, or double ostium, (3) the difficulty in maintaining proper alignment of the coronary cannula during prolonged periods of perfusion, (4) the dog's small, friable, ascending aorta, and (5) complications associated with extracorporeal circulation.

Control Studies.—In the 15 control animals studied (Table I) ventricular fibrillation or cardiac arrest occurred within 8 to 45 minutes after opening the aorta. The electrocardiogram in 5 of these dogs showed regular electrical activity (without ventricular fibrillation) after 60 minutes, even though the heart visibly was in arrest. Coronary artery perfusion was not performed at any time in the control group. Through the open aortotomy of the control animals, we observed that there was always a small, slow flow of blood running from both coronary ostia into the aorta, irrespective of cardiac rhythm. We have made this same observation during other investigations, while employing cardiac arrest and an open aortotomy, in the empty, bypassed heart.

TABLE I. CARDIAC RESPONSE OF 15 CONTROL ANIMALS TO AN OPEN AORTOTOMY WITHOUT CORONARY PERFUSION DURING BYPASS

MEAN TEMPERATURE	ANIMALS STUDIED	MEAN PERIOD BETWEEN OPENING AORTA AND ONSET OF CARDIAC ARREST OR VENTRICULAR FIBRILLATION
31°-33° C.	5	26.0 minutes
33°-35° C.	5	9.2 minutes
35°-37° C.	5	26.0 minutes

Acute Studies.—These 24 experiments were terminated acutely because of technical difficulties encountered during the procedures. Excessive aortotomy bleeding, anatomic variations of the left coronary artery, high plasma hemoglobin, unsuitable coronary cannula tips, and complications of extracorporeal circulation were the major problems in this group. Fifteen of these dogs were studied during the first 25 experiments while a suitable cannula tip was being developed and the operative procedure standardized.

Survivor Studies.—Twenty-two dogs survived from 3 hours to 3½ months (Table II). The early deaths, within 9 days, resulted from: generalized bleeding secondary to cardiopulmonary bypass or postoperative hemorrhage from the aortotomy; sudden death of undetermined cause; infection; cardiac failure; myocardial infarction; and a high plasma hemoglobin (270 to 400 mg. per cent). There was one late death due to empyema.

Continuous perfusion of the left coronary artery was performed, without ventricular fibrillation, for periods of 15 to 60 minutes; the cardiac rate during perfusion varied between 60 and 90. Flows from the coronary cannula (50 ml. to 150 ml. per minute) were measured prior to perfusion but angulation of the cannula plus coronary vascular resistance reduced these initially determined flows. We found the most accurate determination of coronary perfusion was obtained by measuring the total coronary venous return from the right auricle. Total coronary venous flow in the nonworking, bypassed heart, before left coronary artery perfusion, averaged 53 ml. per minute; flows from 40 ml. to 50 ml. per minute proved adequate during perfusion. The suspended reservoir filled with oxygenated blood from the pump permitted coronary perfusion at a constant pressure of 74 to 80 mm. Hg; this was technically preferable to direct perfusion from the arterial line of the pump, although both methods were used successfully in this study.

Results of the mean coronary arteriovenous oxygen differences, expressed in per cent saturation, are summarized in Fig. 2. The bypassed, nonworking heart shows a value of 37.5 per cent which falls to 24.3 per cent (sinus rhythm) and

TABLE II. RESULTS OF THE 22 ANIMALS STUDIED IN SURVIVOR EXPERIMENTS WITH LEFT CORONARY ARTERY PERFUSION ALONE

PERIOD OF SURVIVAL	NUMBER OF ANIMALS	DURATION OF LEFT CORONARY ARTERY PERFUSION (MIN.)	CARDIAC RHYTHM DURING PERFUSION		COMMENTS
			SINUS	VENT. FIB.	*Cause of death*
12 hours or less	4	60	x		Postoperative hemorrhage (aortotomy)
		60	x		Right heart failure
		20	x		Cause undetermined
		17	x		High plasma hemoglobin (270 mg. %)
12 to 24 hours	6	18	x		High plasma hemoglobin (400 mg. %)
		30		x	Right heart failure*
		33		x	Postoperative hemorrhage
		37		x	Right heart failure*
		45		x	Postoperative hemorrhage
		45	x		Postoperative hemorrhage
1 to 9 days	7	15	x		High plasma hemoglobin (400 mg. %)
		24	x		Infarction of right ventricle
		25		x	Empyema (9th day)
		30	x		Complication of pump oxygenator
		30	x		Postoperative hemorrhage
		47		x	Postoperative hemorrhage (aortotomy)
		48		x	Postoperative hemorrhage
6 weeks or longer	5	18	x		Sacrificed at 8 weeks
		20	x		Sacrificed at 6 weeks
		20	x		Sacrificed at 14 weeks
		21	x		Sacrificed at 8 weeks
		23	x		Empyema (6 weeks)

*One dog showed immediate bifurcation and the other immediate trifurcation of the left coronary artery.

24.7 per cent (ventricular fibrillation) during perfusion of the left coronary artery. After unclamping the aorta there is an additional fall to 21.7 per cent in the bypassed heart. The mean oxygen consumption of the entire heart during left coronary artery perfusion was 2.54 ml. per 100 Gm. heart weight per minute in normal sinus rhythm and 2.74 ml. per 100 Gm. heart weight per minute with ventricular fibrillation. In Fig. 2 the results of this investigation are compared with the experimental coronary perfusion studies of others in the totally bypassed, nonworking heart[6] and in the nonworking heart separated from the body as an isolated preparation.[7] The results under these three conditions are essentially the same during adequate coronary perfusion.

Electrocardiographic studies in this investigation demonstrated that when coronary perfusion was inadequate, during the open aortotomy, evidence of myocardial ischemia was present throughout the perfusion period and often persisted until the death of the animal. When adequate coronary perfusion was maintained, however, even during periods of ventricular fibrillation with the aorta open, electrical defibrillation was usually immediate and prompt cardiac recovery followed. None of the long-term survivor animals developed ventricular fibrillation or other significant arrhythmias during their investigation.

DISCUSSION

This study demonstrates several important factors which limit successful left coronary artery perfusion in the experimental animal, and the need for utilizing a special cannula tip to accommodate the dog's left coronary artery.

Adequate left coronary artery perfusion was performed from a suspended reservoir which maintained a pressure above 74 mm. Hg. Jardetzky and associates[5] have shown that a constant perfusion pressure of 65 mm. Hg furnishes an adequate coronary flow, with an unaltered oxygen consumption for 3 hours, in the isolated, empty, nonworking, dog's heart with sinus rhythm.

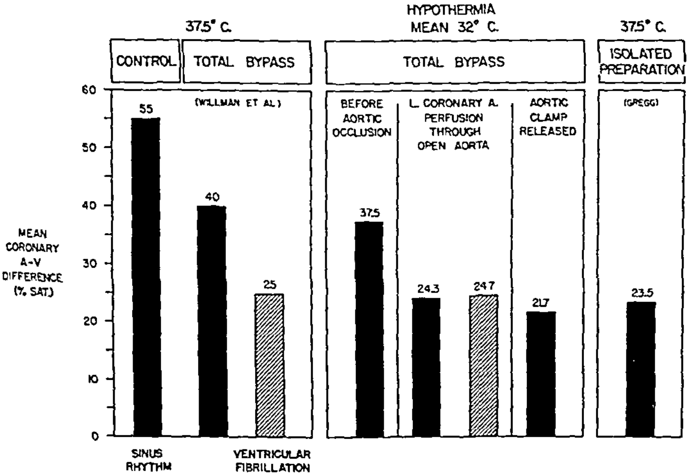

Fig. 2.—Coronary arteriovenous oxygen differences of this study are shown in the *middle* section and are compared with results from the investigation of Willman et al.[6] (totally bypassed closed heart) and studies summarized by Gregg[7] (isolated heart preparation). All are studies in the dog heart. Normal sinus rhythm is shown in solid black and ventricular fibrillation by cross-hatching.

Continuous left coronary perfusion *alone* was performed from 15 to 60 minutes in this investigation without fibrillation. Shumway[2] has reported similar results during 15 minutes of left coronary artery perfusion. We found during prolonged periods of ventricular fibrillation, with adequate left coronary artery perfusion, that electrical defibrillation was immediate and cardiac recovery prompt. These findings have been substantiated clinically and apparently ventricular fibrillation during an open aortotomy is not harmful, providing the coronary vascular bed is *adequately perfused.*

The mean coronary arteriovenous oxygen differences (using animals of about equal size), during adequate left coronary artery perfusion at an average temperature of 32° C., were the same in the presence of ventricular fibrillation or a normal sinus rhythm (Fig. 2). Willman, Neville, and Hanlon[6] reported similar values in the normothermic, nonworking, bypassed, dog's heart, without an aortotomy; both coronary arteries were perfused normally in their investigation. Gregg's[7] summary of studies in the normothermic, isolated, nonworking, canine heart with sinus rhythm showed the coronary arteriovenous oxygen difference to be approximately the same as the open, nonworking, left coronary perfused hearts during sinus rhythm of this investigation (Fig. 2).

The myocardial oxygen consumption during left coronary artery perfusion of the nonworking, open heart, in this experimental study, was the same with fibrillation or normal sinus rhythm. Beuren, Sparks, and Bing[8] found no statistical difference, in the closed chest dog, between the oxygen consumption of the artificially perfused, empty heart during sinus rhythm or ventricular fibrillation.

SUMMARY AND CONCLUSIONS

1. Continuous left coronary artery perfusion alone may be performed for prolonged periods through an ascending aortotomy without ventricular fibrillation. This procedure is frequently limited by the anatomic variations of the dog's left coronary artery.
2. Arterial perfusion which provided a total coronary venous return of 40 ml. to 50 ml. per minute was adequate in the nonworking heart with an ascending aortotomy.
3. Coronary artery perfusion from a suspended reservoir at a constant pressure of 74 to 80 mm. Hg was preferable to arterial perfusion from the pump, although both methods were used successfully.
4. Coronary arteriovenous oxygen differences and oxygen consumption in the nonworking dog's heart, during left coronary perfusion through an aortotomy, were approximately the same with normal sinus rhythm and ventricular fibrillation.
5. The long-term survivor animals did not develop fibrillation during their investigation. However, in other dogs, when adequate coronary artery perfusion was maintained during periods of ventricular fibrillation, electrical defibrillation was immediate and cardiac recovery prompt.
6. The most important single factor contributing to cardiac recovery during an open aortotomy in this investigation was *continuous adequate coronary perfusion,* irrespective of variations in temperature, cardiac rhythm, and the method or duration of perfusion.
7. Clinically left coronary artery perfusion, performed from the arterial line of the pump through an ascending aortotomy, has proved very satisfactory regardless of the duration of perfusion. In the experimental animal, prolonged left coronary artery perfusion may be a complicated procedure and is difficult to execute consistently with success.

We wish to express our appreciation to Mr. Thomas Perry, Mr. Eugene Varga, Mrs. Mary E. Garrard, and Mr. Boyd Perry for their technical assistance.

REFERENCES

1. Muller, W. H., Jr., Warren, W. D., Dammann, J. F., Jr., Beckwith, J. R., and Wood, J. E., Jr.: Surgical Relief of Aortic Insufficiency by Direct Operation on the Aortic Valve, Circulation 21: 587, 1960.
2. Shumway, N. E.: Forward Versus Retrograde Coronary Perfusion for Direct Vision Surgery of Acquired Aortic Valvular Disease, J. THORACIC SURG. 38: 75, 1959.

3. Melrose, D. G.: Discussion *in* Extracorporeal Circulation, Springfield, 1958, Charles C Thomas, publisher, p. 498
4. Headrick, J. R., Strayhorn, W. D., Munoz, A. J., and Adams, J. E.: A Method of Safely Prolonging Induced Cardioplegia, S. Forum 10: 509, 1959
5. Jardetzky, O., Greene, E. A., and Lorber, V.: Oxygen Consumption of the Completely Isolated Dog Heart in Fibrillation, Circulation Res. 4: 144, 1956
6. Willman, V. L., Neville, E. C., and Hanlon, C. R.: Cardiac Metabolism Under Conditions Associated With Open Heart Operations. I. Coronary Sinus Flow and Myocardial Oxygen Consumption, S. Forum 8: 287, 1957
7. Gregg, D. E.: Coronary Circulation in Health and Disease, Philadelphia, 1950, Lea & Febiger, p. 154
8. Beuren, A., Sparks, C., and Bing, R. J.: Metabolic Studies on the Arrested and Fibrillating Perfused Heart, Am. J. Cardiol. 1: 103, 1958

(For Discussion, see page 699)

THE GROWTH OF CARDIOVASCULAR CHAMBERS FOLLOWING CARDIAC AND AORTIC SURGERY

Sigmund A. Wesolowski, M.D. (by invitation), Lester R. Sauvage, M.D. (by invitation), Philip N. Sawyer, M.D. (by invitation),** Karl E. Karlson, M.D., and Lester Fox, M.D. (by invitation),*
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THE DEVELOPMENT of intracardiac surgery for the correction of human congenital cardiac defects has been so rapid as to outstrip the available knowledge from the experimental laboratory concerning the long-term fates of the intracardiac procedures performed. This communication presents the results of our initial characterization of the growing pig preparation which we feel gives equivalent long-term results very rapidly. In this preparation all cardiac and vascular diameters double in a 6-month period of maturation, "degenerative" calcific changes occur in or around implants during this 6-month period, and this preparation has proved to be a very sensitive indicator of aberrations in the outflow tracts of the ventricles and great vessels.

METHOD

Left Ventricular Studies.—The present report includes 209 pigs bearing 5.5 cm. long, isodiametric grafts of various materials which replaced resectional defects of the descending thoracic aorta. These grafts were implanted at pig body weights of from 14 to 44 pounds (10 to 12 weeks of age). Pigs were allowed to mature for 6 to 12 months to be slaughtered at an average body weight of 235 pounds. At slaughter, the heart and thoracic aorta were removed from each animal; the aorta containing the graft was x-rayed after inflation with air at 120 mm. Hg pressure. Details of the fates of these grafts will be published elsewhere.[5] Measurements of internal diameters were taken from the roentgenograms: graft diameter used was the minimum internal diameter while the distal aortic diameter used was the largest diameter between the distal end of the graft and the first patent intercostal artery. In the stenotic grafts, poststenotic dilatation was corrected for as shown in Fig. 1. The hearts of these

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*Third Research Scholar, American College of Surgeons.

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same animals were trimmed in the fresh state as follows: the right ventricle was cleanly excised from the atrium at the tricuspid valve ring and from the ventricular septum and included that portion of the pulmonary artery bearing the sinuses of the pulmonary valves; the left ventricle included the ventricular septum but excluded the entire aorta and atrium at the aortic and mitral valve rings, respectively. The cavities and muscular trabeculae were cleaned of all thrombi and each ventricle separately weighed. Good reproducibility of this ventricular trim technique in our hands is demonstrated in Table I and has independently been reported by Busch[2] as a valid technique for studying the human heart.

TABLE I. VENTRICULAR TRIM—NORMAL ADULT PIG HEART

OBSERVER	NUMBER OF HEARTS	MEAN RV LV	STANDARD DEVIATION
S. A. W.*	6	33.5%	± 1.8%
S. A. W.*	19	31.9%	± 1.8%
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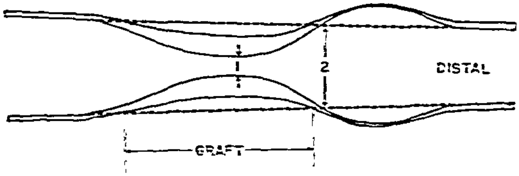

Fig. 1.—Diagram of the method for correction of diameter relationship in the presence of post-stenotic dilatation. The dotted lines represent the normal aortic taper in the absence of stenosis or post-stenotic dilatation. Corrected percentile patency, therefore, is equal to diameter at 1 / diameter at 2 ×100 per cent.

Right Ventricular Studies.—This report also includes 11 other pigs in which one of four different right ventricular outflow tract aberrations was created at the standard pediatric age: 2 pigs had simple resection of one pulmonic valve cusp using a partial occlusion technique; 2 pigs had simple elliptical excision of a portion of the infundibulum, one pulmonic valve cusp and sinus with simple closure and bicuspidization of the pulmonic valve using a partial occlusion technique—the average systolic gradient produced by this degree of stenosis at operation was found to be 8 mm. Hg; 2 animals had simple elliptical excision as above and replacement of the excisional defect with an isometric Ivalon patch of 8:1 compression ratio; the remaining 5 animals had elliptical excision with isometric replacement of the excisional defect with autologous fibrous pericardium. Patch replacements were accomplished using moderate depth immersion hypothermia and inflow-occlusion for 3 to 5 minutes; these patches averaged 2.7 by 2.0 cm. at implantation. These animals were allowed to mature (as above). At slaughter, the heart was removed, x-rayed in the anteroposterior and lateral projections with the pulmonary artery and right ventricle inflated with air at a pressure of 30 mm. Hg. The ventricles were individually trimmed and weighed as above.

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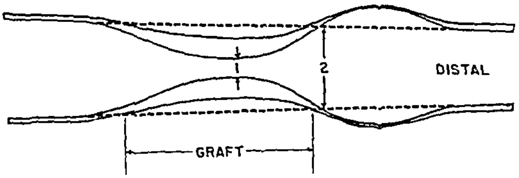

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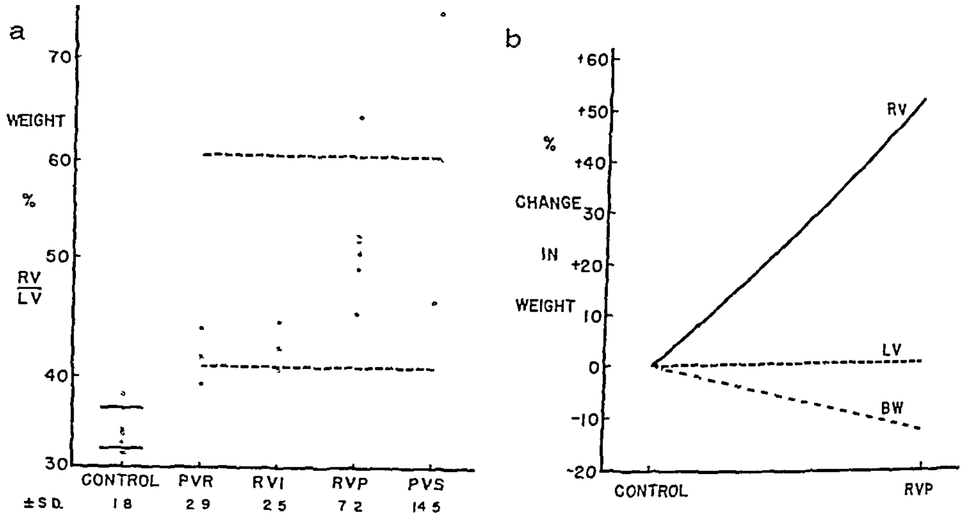

Fig 2 —*a* Graph which plots percentile RV/LV weight ratios for various right ventricular outflow tract aberrations Controls are 6 pigs with no cardiovascular lesions *PVR* = 1 cusp pulmonic valve resection *RVI* = Ivalon patch in right ventricular outflow tract. *RVP* = free autologous pericardial patch in right ventricular outflow tract *PVS* = elliptical excision of one cusp of pulmonic valve with bicuspidization of remaining valve The solid black lines in the controls represent values of ±1 SD whereas the dotted lines represent values of ±1 SD for the entire group of pigs with right ventricular outflow tract aberrations Note that there is no overlap of the two sets of standard deviations

b Graph which demonstrates the percentile increases over control values of the weights of the right ventricle left ventricle and total body in pigs bearing free pericardial patches replacing elliptical excisions of one pulmonic-valve cusp All control and RVP pigs were mature at the time of slaughter the pericardial patches had been inserted at 12 weeks of age

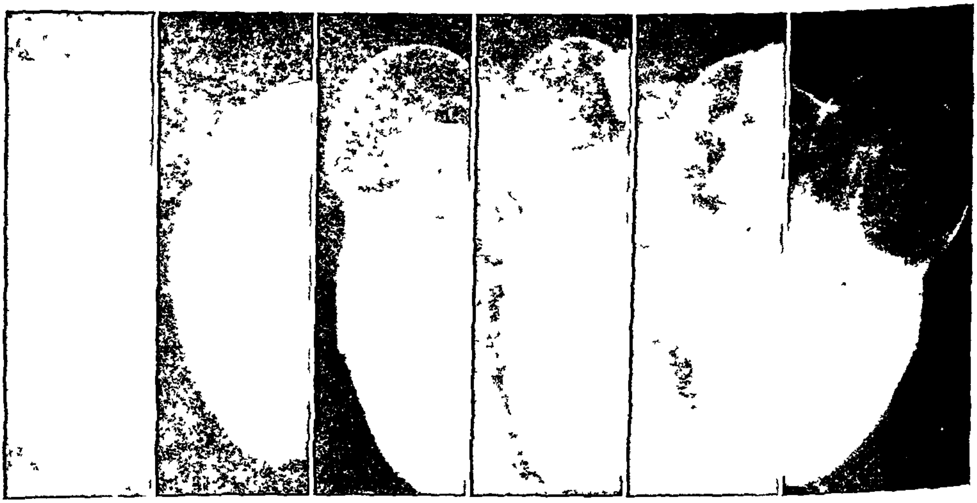
A. *B.* *C.* *D.* *E.* *F.*

Fig 3 —Lateral roentgenograms of the right ventricular outflow tract and main pulmonary artery of the hearts of pigs All pigs were operated upon at about 30 pounds of weight and all were mature (*200* pounds or more) except in *B* (*76* pounds) at death or sacrifice Tract in *B* filled with Diodrast all others inflated with air at 30 mm Hg pressure *A*, Normal adult pig *B* Resection 1 cusp pulmonic valve note increased trabeculation of right ventricle *C*, Elliptical excision of 1 cusp with bicuspidization of the pulmonic valve note preservation of same degree of stenosis with growth and post stenotic dilatation of pulmonary artery here and in *D* *D* Elliptical excision with Ivalon patch replacement with development of slight stenosis with growth because of the inability of growth of the Ivalon patch, note also calcification of the Ivalon patch verified by histologic examination *E*, Elliptical excision with free pericardial patch replacement with preservation of relatively normal diameter relationships with growth *F* same as *E* but with aneurysmal dilatation of pericardial patch

RESULTS AND CONCLUSIONS

There is a gross correlation between age and ventricular weights, but the ratio of the individual weights of the ventricles (RV/LV) of all animals beyond 20 weeks of life was found to fall within the normal adult ratios listed in Table I. The RV/LV weight ratio was used, therefore, as the cardiac parameter to be studied.

Right Ventricular Studies.—In all 11 animals with minimal right ventricular outflow tract aberrations there was a significant increase in the RV/LV weight ratio as summarized in Fig. 2, *a*; this increase was due to increase in the RV weight over control values as summarized in Fig. 2, *b* which also demonstrates that the ventricular changes are independent of body weight. Eight of these animals and the 6 control animals with no outflow tract aberrations were slaughtered between 5 to 6 months after operation. Three animals died as follows: 1 with pulmonic valve regurgitation died of pneumonia 118 days after operation, another with the same lesion died of large bowel obstruction caused by rectal prolapse at 134 days, and the third, with stenosis, died *with congestive heart failure* 36 days after operation. The gross changes in the right ventricular outflow tract are summarized in Fig. 3. Space does not permit the detailed description of these changes but suffice it to say that pulmonary valve stenosis or regurgitation of a degree considered to be clinically insignificant produces ventricular changes easily detectable in the preparation of the growing pig within a 6-month period of maturation.

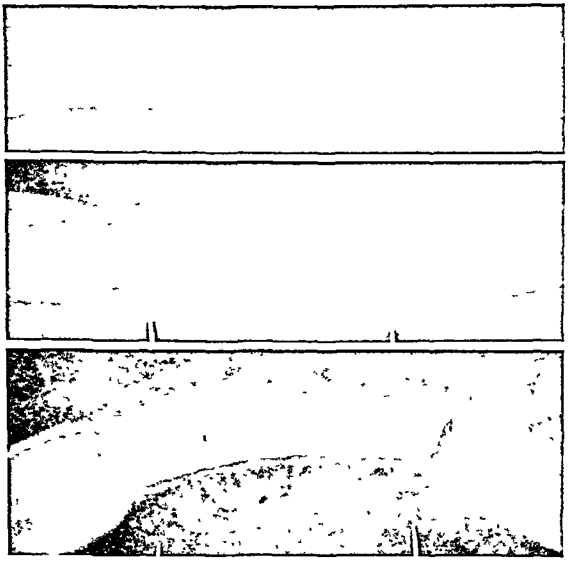

Fig. 4.—Roentgenograms of examples of graft stenosis at coarctation site. Specimens inflated with air at 120 mm Hg pressure *Upper*, aortic autograft with 100 per cent patency (0 per cent stenosis) *Middle*, prosthetic graft with 50 per cent patency. *Lower*, prosthetic graft with complete occlusion or 0 per cent patency Note the calcific changes within the latter prosthetic graft.

Left Ventricular Studies.—In the 209 animals implanted with various kinds of isodiametric grafts to replace defects in the upper descending thoracic aorta, varying degrees of graft stenosis were observed to occur consequent to maturation. Examples of graft stenoses are shown in Fig. 4. The RV/LV weight ratio was proportionately lowered at graft diameters less than 50 per cent of the average adult pig aortic diameter at the standard graft site (Fig. 5). When the degree of stenosis was corrected for varying aortic diameter (and also for post-stenotic dilatation as shown in Fig. 1), the RV/LV weight ratio is shown to decrease at *all* degrees of stenosis, even at high patency values (graft diameter/distal aortic diameter), as demonstrated in Fig. 6, *a*. That the lowering of the RV/LV weight ratio is due to increase in the left ventricular weight below 80 per cent graft patency values is demonstrated in Fig. 6, *b*. Indeed, below 60 per cent patency there is a smaller and concomitantly progressive increase in the right ventricular weight. This rise in right ventricular weight is of a lower order of magnitude than the left ventricular rise and may well be due to an elevated end diastolic left ventricular pressure (and therefore elevated pulmonary circuit pressure) consequent to left ventricular hypertrophy. It is sufficient to the purposes of this communication, however, to point out that there are easily detectable effects upon the heart of even mild degrees of stenosis of the outflow tract of the left ventricle even at some distance removed from the aortic valve, such as in the upper descending thoracic aorta. These changes with growth of the animal can be detected within a 6-month period of observation.

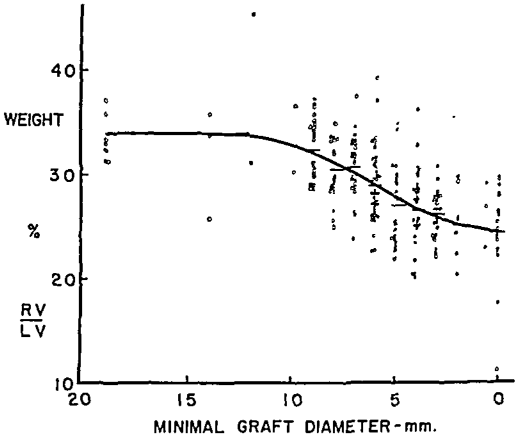

Fig. 5.—Graph which plots percentile weight RV/LV against minimal graft diameter. From simple observation of these data it would seem that there is no aberration of the RV/LV weight ratio until the stenosis is less than 10 mm. which apparently is about 50 per cent of the normal aortic diameter at this site.

DISCUSSION

What is the significance of aneurysm formation of autologous pericardium implanted into the outflow tract of the right ventricle? In the pig the fibrous pericardium is much more flimsy than in the dog and human being. This is demonstrated by the fact that free autologous pericardial implants used to replace thoracic aortic defects in the growing pig[5] rupture within a week after operation, whereas those in the adult dog[4] remain intact for periods of 18 months or more without rupture or aneurysm formation.

What is the significance of ventricular hypertrophy? Certainly lesions that produce marked degrees of ventricular hypertrophy can be lethal and it would seem reasonable to assume that minimal degrees of hypertrophy are innocuous. Moderate degrees of ventricular hypertrophy, as found in this study, are well tolerated on short-term follow-up but we have no data as to the relationship of moderate ventricular hypertrophy to longevity or to increased susceptibility to angina pectoris on long-term follow-up. Without entering into a discussion of surgical philosophy, the procedure which leads to less ventricular hypertrophy would be the preferable. It is suggested that choice of intracardiac procedure

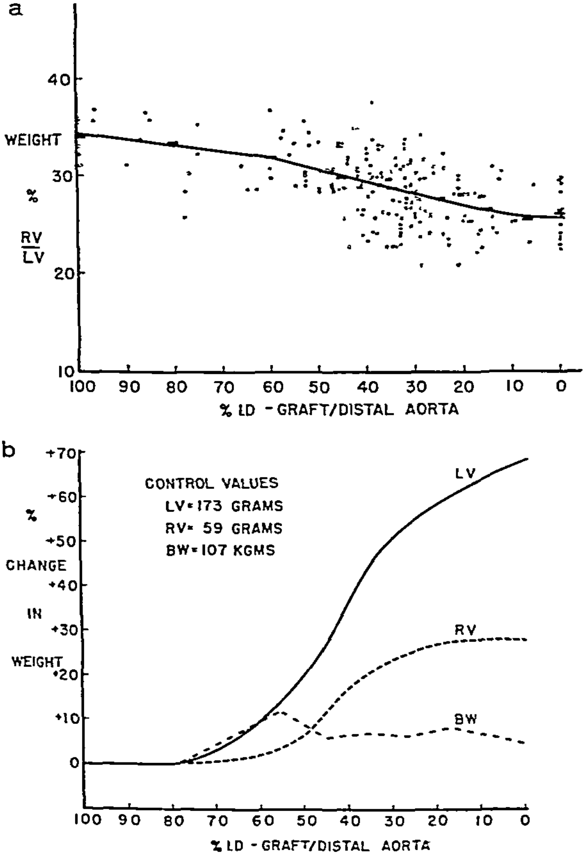

FIG. 6.—*a*, Graph which plots percentile weight RV/LV against percentile patency which corrects for varying aortic diameter distal to the site of stenosis. With such correction, even mild degrees of stenosis in the coarctation site are detected by the RV/LV weight ratio. *b*, Graph which plots percentile deviation from control values of ventricular weights against percentile patency of grafts at the coarctation site. Note that the left ventricular weight increases at patency values below 80 per cent and that a smaller percentile increase in right ventricular weight occurs at patency values below 60 per cent.

could be accurately and rapidly screened in the growing pig preparation and, thus, accelerate the progress of intracardiac surgery.

What is the significance of calcification of Ivalon implants into the heart? The report of Blumberg, Griffith, and Merendino[1] that Ivalon implants in the human can calcify, become rigid, and erode an aortic valve leaflet demonstrates that calcification of a prosthetic may be undesirable. The present communication demonstrates that the preparation of the growing pig can detect calcific deposit in prosthetic cardiac implants within a period of 6 months.

SUMMARY

1. Lesions simulating clinically minimal pulmonic stenosis, pulmonary valve regurgitation, and right ventricular outflow tract widening, using patches of Ivalon or autologous fibrous pericardium, have been produced in growing pigs. The pigs were allowed to mature.

2. In a large series of growing pigs, defects of the thoracic aorta were bridged, using various graft materials. At maturity these grafts were found to be variously stenosed.

3. The right ventricular weight and RV/LV weight ratio were found to be moderately elevated over control values in all of the mature pigs bearing minimal right ventricular outflow tract aberrations.

4. Ivalon implants in the outflow tract of the right ventricle produced mild stenosis with growth and attracted calcific deposit while free autologous fibrous pericardial implants formed aneurysms.

5. Stenosis at the thoracic aortic coarctation site produced increase in left ventricular weight and decrease in the RV/LV weight ratio when compared to control values. These changes were observed when the stenosis was greater than 20 per cent. (Less than 80 per cent patency.) Lesser increases in right ventricular weight were also observed at diameter ratios less than 60 per cent; the latter increases did not correlate with differences in age or body weight of the animals.

6. It is concluded that the growing pig can be used as a sensitive preparation for the rapid screening of the comparative hemodynamic effectiveness and expected clinical worth of cardiac and thoracic aortic surgical procedures. It is further suggested that, in addition to such screening, certain other species-transferable data, such as calcification of cardiovascular implants, can be concomitantly gained.

REFERENCES

1. Blumberg, Y. B., Griffith, P. C., and Merendino, K. A.: The Effect of Specific Compression on Soft-tissue Response to Formalinized Polyvinyl Alcohol (Ivalon) Sponge, Ann. Surg. 151: 409, 1960.
2. Busch, W.: New Measurements of the Thickness and Weight of the Ventricles in Various Forms of Hypertrophy, With Special Consideration of the Histologic Findings, Arch. Kreislaufforsch. 22: 267, 1955; Abstr. Circulation 15: 141, 1957.
3. Moss, A. J., Adams, F. H., O'Loughlin, B. J., and Dixon, W. J.: The Growth of the Normal Aorta and of the Anastomotic Site in Infants Following Surgical Resection of Coarctation of the Aorta, Circulation 19: 338, 1959.

4 Sauvage, L R, and Gross, R. E. Three Year Results of Autologous Pericardial Grafts in Canine Thoracic Aorta. 1960. (Unpublished data.)
5 Wesolowski, S A.: Evaluation of Tissue and Prosthetic Vascular Grafts Monograph to be published by Charles C Thomas, publisher, Springfield, Ill.

DISCUSSION

(PAPERS BY BURMAN [PAGE 635], LONG [PAGE 640], SMYTH [PAGE 653], GILBERT [PAGE 667], TAKARO [PAGE 673], LITTLEFIELD [PAGE 685], WESOLOWSKI [PAGE 692], AND THEIR ASSOCIATES)

DR CHARLES ROSS, Buffalo, N. Y—The use of nitrogen mustard in the management of bronchogenic carcinoma has been studied for the last 2½ years by a cooperative group There were 22 investigators participating in this study

The nitrogen mustard was given at the time of surgery, initially in a dose of 0.4 mg; later, when the study became a double blind study, in the amount of 0 3 mg/Kg

The complications were higher The mortality rates were identical in the two groups. This slide is a life table analysis of survival, and the 2½ year survival is 30 per cent. There is identical survival in the treated as well as the control group

So we can surmise that nitrogen mustard used in this fashion will not prolong survival in the surgical treatment of bronchogenic carcinoma

DR PAUL NEMIR, JR, Philadelphia, Pa—It is our opinion too that this method of regional perfusion is a reasonable one in nonresectable carcinoma of the lung, and have had occasion to use it

[Slide] This slide is of a 60 year old man with undifferentiated carcinoma of the right lung and mediastinal metastases We gave this man 0 4 mg./Kg of nitrogen mustard in 33 ml with 4 mg of Renografin, and kept the balloon occluded for a period of 12 minutes On this film, taken at 7 minutes after the administration of cancericidal agent, you can still see the contrast material in the lung vasculature

The patient experienced an extreme hot flush on the right side of the chest during the period of occlusion As soon as the balloon was deflated, he experienced the generalized hot flush that one gets with nitrogen mustard in a single dose. While there may have been slight leakage, we consider this supporting evidence that the cancericidal agent remained fairly well localized for a period of 12 minutes

It has now been about 3 weeks since the perfusion We believe that there has been a definite regression in the size of the lesion in the lung, but we have run into the same difficulty that Dr Smyth reported

[Slide] This is the chest film taken 48 hours after perfusion You can see the chemical pneumonitis that has occurred in the right lower lobe This has been clearing, but what the final status will be, we don't know

We are in the midst of studying experimentally the effect of cancericidal agents on the vessels I think that it is encouraging that there has been some decrease in the size of the lesion in the lung

DR HARRIS B SHUMACKER, JR, Indianapolis, Ind—Although I have had no opportunity clinically to utilize grafts from the right ventricle to the pulmonary artery, I thought you might be interested in an unusual case in which a graft was interpolated between the pulmonary trunk and one main pulmonary artery.

This was a case of an 11 month old child who had done very badly. He had episodes of intermittent cyanosis and very poor weight gain During his admission to the hospital he lost weight in spite of the best medical treatment. X ray studies showed evidence of right ventricular hypertrophy and increase in pulmonary vasculature

The first catheterization study had to be carried out with continuous administration of oxygen, and was not entirely satisfactory, but a subsequent one was more satisfactory. At the second catheterization the femoral artery saturation was only 52 per cent without oxygen, but rose to relatively normal levels with administration of oxygen The pressure in the pulmonary trunk was equal to that in the aortic arch The left main pulmonary artery arose from the pulmonary trunk, the right from the aortic arch, and there was a large patent ductus with generous angiographic reversal of flow These anomalies were demonstrated by cine angiography.

At operation the very large right pulmonary artery was detached from the aortic trunk, and a Dacron graft was interpolated between the side of the pulmonary trunk and the right main pulmonary artery This went smoothly It was done as a closed procedure and the results so far have been very gratifying. Prior to operation the patient weighed 14½ pounds When seen 5 weeks later, symptoms had disappeared The child seemed to be quite well, and had gained 4½ pounds during the 5 weeks' time The child will be recatheterized within the next few weeks

This case demonstrates that it is possible to obtain a good result with a plastic prosthesis to the pulmonary artery

DR THOMAS C MOORE, Indianapolis, Ind.—We became interested in the problem of pulmonary artery replacement following the interesting paper which was presented before this Association 2 years ago by Robinson and his associates Since that time we have replaced the proximal left pulmonary artery in 50 animals, utilizing a variety of grafts We have used fresh autogenous systemic artery, fresh autogenous systemic vein, and crimped Teflon vascular grafts The patency in all has been quite satisfactory

The animals have been observed from 6 to 391 days following operation Ten of 14 systemic arterial grafts remained patent Seventeen of 19 venous grafts remained patent, and 16 of 17 Teflon grafts remained patent

The patency has been encouraging to us, and has been substantiated by our observations with another type of replacement in the superior vena cava, in which we have carried out 78 grafts, using sizes significantly smaller to significantly larger We have encountered a patency of 86 per cent in the last 50 consecutive grafts We have also found that all of those which remained patent past an early critical period tended to remain patent

We also have carried out operations similar to those reported by Dr Gilbert, employing Teflon grafts from the pulmonary artery to the right ventricle This has been employed in 12 animals, and the patency has not been quite as satisfactory as his We have encountered graft occlusion in right ventricular anastomosis in a number of animals

DR ADRIAN KANTROWITZ, Brooklyn, N Y—During the summer of 1959 I had an opportunity to visit the first thoracic surgery hospital in Moscow, and, subsequent to this, Dr Kolyesnikov, who is the Director of this unit, sent me a stapling device which was designed to staple the auricular appendage I thought it might be of some interest to see what this device looks like

I have a short 2 minute movie which I would like to show [A film was started]

The instrument comes in this wooden box, which is plush lined, and consists of several parts the stapler itself, a container with two extra magazines, and a small box which contains the tantalum staples The staples are small and sharpened They measure about 4 mm by 4 mm The two extra magazines are identical, and it comes apart very simply, like this

First the driving nut is placed on one end of the jaw This is the staple advance apparatus The second part of the jaw snaps into position, and the handle just simply clicks into place

The magazine, containing two lines of eight staples, is simply fixed, on one side of the jaw, and then by simply squeezing the handle the staples are put into position

Here, demonstrating on a small piece of gauze, the jaws are closed and the staples are driven home Here is the double row of staples, and this is the obverse side, and on the inside, one can see a nice seal

This is a patient in which we had just completed doing a commissurotomy The stapling apparatus is placed just below the Satinsky clamp, and the jaw is advanced, the safety device is opened, and the jaws closed

Here you can see the double row of staples placed at the base of the left auricular appendage.

DR. KIYOSHI INOKUCHI, Kyushu, Japan.—I am very interested in Dr. Takaro's speech, since several years ago I also worked out a device on the mechanical suture of blood vessels. This involved the multiple stapling of everted vessels with special steel clips. A description of my end-to-end apparatus was published in the *Archives of Surgery* in 1958.

[Slide] Last year I devised a side-to-end apparatus and successfully applied it to 7 patients during splenorenal shunts.

[Slide] Later I constructed another type which is specifically applicable and convenient for end-to-end anastomosis of large vessels. It is of a different type from that described by Dr. Takaro.

[Slide] Some people may be suspicious that the device is only good for laboratory experiments, and that it would be hardly applicable to clinical cases. However, I disagree with such an opinion because of my previous experiences. In long-survival experiments in 135 dogs, there were only three failures from thrombosis. There was none from anastomotic insufficiency.

The results from grafting of a small artery, as shown here, showed only two failures in 34 cases, in contrast to the results from the use of the manual suture, in which there were eight failures in 15 cases.

[Slide] Homologous vein transplantation of the portal vein showed no failures in 9 cases, while there were 4 cases of failure in ten instances when the manual suture was used.

[Slide] So far, I have used my end-to-end stapling device in 22 patients with satisfactory results. Particularly, I should like to point out that the apparatus was also applied to sclerotic, thickened vessels, without many technical difficulties or mishaps.

I believe that a well-designed multiple stapling device can overcome the difficulties in patients with the manual suture, and that it is able to make a good contribution to vascular surgery.

DR. HENRY T. BAHNSON, Baltimore, Md.—We agree with Dr. Littlefield that coronary perfusion is good and necessary. Even when using hypothermia, we continue to use perfusion lest we fall into the same trap as the band wagon of potassium citrate from which most of us have recently alighted.

It is difficult to transfer conclusions from the dog to man, because of the very small size of the right coronary artery. We believe both arteries should be perfused in the human being. This is more trouble [slide] than not perfusing them, obviously.

We have found that the catheters shown here are the easiest of the several types that we have used. We continue to use perfusion cannulas like the one that Dr. Littlefield showed, after the suggestion of Dr. Muller. In most instances, however, this catheter, patterned after one that Dr. Starling used in coronary perfusion many years ago, has worked satisfactorily. These have metal tips on them plus a small balloon and a plastic catheter.

They are relatively easy to insert and are held in with a suture. The balloon is inflated with saline, and when the catheter is removed, this is deflated. We have used them for periods up to 80 minutes with good maintenance of cardiac tone and resumption of cardiac activity when the circulation is restored.

[Slide] We have used this particularly in regard to cusp replacement, although they have also been used in valvuloplasty and removal of calcium from the aortic leaflets. This shows the method of making the cusps which we have used. This is Teflon fabric formed over a mold. When the knitted fabric is heated to 500° F., the plastic assumes the shape of the mold, and one ends up with a cusp like the one shown in the next slide.

[Slide] We have tried to replace all three cusps in a single patient, without success. One of our difficulties has been, I believe, in determining the proper size of these cusps. It is much simpler when only a single cusp is contemplated, and we believe in many instances, if not most instances, use of a single cusp will probably carry the patient along at least until our technical advances catch up with the patient's disease

We have used these in 4 patients. With 3 there has been dramatic improvement The fourth patient died a week later of a myocardial infarction.

The end result looked very much like the silicone coated cusp which Dr. Hufnagel showed It was more flexible than the adjacent cusp, on which we had done a valvuloplasty

DR. CHARLES P. BAILEY, New York, N. Y.—Perfusion of two coronaries is generally better than that of one. However, there is a great variation in human cases, and, in some, the intercoronary collaterals apparently may serve us well, as in cases in which there is difficulty in cannulating the right coronary artery.

[Slide] The right coronary artery sometimes bifurcates almost immediately after its origin, so cannulation may be difficult. This is the equipment we have used, two polyethylene tubes with sponge rubber carrot like cuffs which are inserted as shown on the next slide

[Slide] The left coronary cannula is affixed by an encircling purse string suture placed within the aortic lumen; the right one by a suture passed externally around the right coronary artery. We tried tubing and spring like devices but have come to not use them. First, they get in the way of the surgeon, and, second, if the aortic incision is made close to the right coronary ostium, a strong assistant holding a metal cannula may pull the coronary artery completely off the aorta This creates a very difficult problem. [Laughter]

Another thing we have found is that flow rates required in these cases are larger than one would expect. Naturally, these operations are performed for aortic disease, usually stenosis or insufficiency, and the heart is much larger than normal No doubt the coronary circulation is less adequate than usual. We have found that a flow of 200 or 300 c c a minute usually is not enough for an adult at normothermic temperatures and have had to increase it up to 1,000 c c per minute in some instances

Studies on dead hearts in patients of this type, and studies at the operating table, suggest that the desired flow rate is infinitely variable and should be monitored by measuring the pressure within the coronary artery. This may be obtained by direct needle puncture—as distally in the coronary tree, of course, as is feasible We think the coronary arterial pressure should be kept at about the level of the systemic arterial perfusion pressure We urge that both coronaries be used whenever possible.

However, if there is a retrograde perfusion flow of dark blood from the right coronary ostium when the left is perfused, that patient probably has good enough intercoronary collaterals to get along, especially if the time of aortotomy is going to be reasonably short

Announcements

THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

Notice of Annual Meeting

The Forty-first Annual Meeting of The American Association for Thoracic Surgery will be held April 24, 25, and 26, 1961, in Philadelphia, Pennsylvania. Headquarters will be the Sheraton Hotel.

Requests for Hotel Reservations

These should be mailed directly to Mr. Brian Kirby, Reservation Manager, Sheraton Hotel, Philadelphia 3, Pennsylvania. Please mention this Association, the type of accommodation desired, the date, and approximate hour of arrival and departure. If accommodations are desired elsewhere please communicate directly with the hotel of your choice.

Material for the Program

SCIENTIFIC PAPERS.—Abstracts of all papers proposed for presentation at the 1961 meeting *must be received on or before* **November 15, 1960,** otherwise they will not be considered by the Program Committee. These should be labeled "For Thoracic Surgery Forum" or "For Regular Program" depending upon the nature of the subject matter, in the same manner as in previous years. They should contain from 200 to 250 words that accurately reflect the content of the completed paper.

Six, repeat, six clearly legible copies of *each* abstract must be sent to Miss Ada Hanvey, Administrative Assistant, The American Association for Thoracic Surgery, 308 Carondelet Building, 7730 Carondelet Avenue, St. Louis (Clayton) 5, Missouri.

Essayists selected for the program are reminded that papers presented at the meeting *must* be handed to the secretary *immediately* after their presentation. If they are not ready at that time there is a chance that they will not be published in THE JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY.

Applications for Membership

Applications for Associate Membership in the Association must be received by the Membership Committee *not later than* **November 15, 1960,** otherwise the application will be deferred for consideration until the 1962 meeting.

Applicants must be sponsored by three Active or Senior Members of the Association. In addition to the signature on the application form, the sponsors will forward a *separate* letter concerning the applicant directly to:

Frank Gerbode, M.D.
Chairman of the Membership Committee
Presbyterian Medical Center
San Francisco 15, California

Sponsors are reminded that *new* letters of recommendation must be forwarded to the Chairman of the Membership Committee should their applicants be held over for reconsideration a *second year.*

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Original Communications

COARCTATION OF THE AORTA WITH PARTICULAR EMPHASIS UPON IMPROVED TECHNIQUES OF SURGICAL REPAIR

George C. Morris, Jr., M.D. (by invitation), Denton A. Cooley, M.D.,
Michael E. De Bakey, M.D., and E. Stanley Crawford, M.D.,
Houston, Texas

DURING the 15-year period since successful surgical correction of coarctation of the aorta was first reported, extensive experience with this lesion has provided the basis for new concepts of surgical repair.[5, 10] Anatomic and physiologic variations of this congenital anomaly have received intensive study as a direct result of this surgical interest.[1, 2, 3, 9, 12, 13, 14, 16, 19, 22] Equally interesting in certain respects have been observations of acquired pathologic changes resulting from abnormal hemodynamics produced by the coarctation.[8, 17, 18, 20, 21] Ideal technical correction of this disorder must, on the one hand, take into account anatomic variations in location and extent of the process to establish normal aortic hemodynamics and, on the other hand, treat any acquired pathologic changes, such as local arteriosclerosis and aneurysm formation (Fig. 1). When surgical treatment was first introduced, limitations were placed upon selection of patients for operation based upon age, length of aortic occlusion, presence of associated pathologic lesions, such as atheromatous or aneurysmal disease, and other factors. In general, the primary

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Read at the Fortieth Annual Meeting of The American Association for Thoracic Surgery at Miami Beach, Fla., May 11-13, 1960.

objectives of therapy have been removal of the lesion and restoration of aortic continuity. As emphasized previously, however, certain modifications in this concept have evolved, influenced largely by the pathologic variations in the disease.[6] Since the major problem in this condition is concerned with hemodynamic disturbances produced by the occlusive process, the primary objective of therapy is correction of these disturbances with restoration of normal circulation. This may be achieved in most forms of the disease by extirpation of the coarcted segment with end-to-end anastomosis or with graft replacement (Fig. 2). In those associated with aneurysmal formation, extirpation of the lesion is essential. But in some of the more unusual types, particularly those associated with relatively long coarcted segments or with severe arteriosclerotic or calcific changes, the primary objective of therapy, that is, restoration of normal circulation, may be readily achieved by means of the bypass graft without removal of the lesion, thus avoiding some of the difficulties and hazards associated with excision and graft replacement (Fig. 3). In light of these observations this report is concerned with consideration of application of these concepts of surgical treatment and an analysis of our experience in a series of 171 cases of coarctation in which they were employed.

PROCEDURES USED

End-to-End Anastomosis.—In general, direct suture, with establishment of aortic continuity after resection of coarctation, has been employed most commonly for patients in the first two decades of life with short "adult" or postductile type stenosis (Fig. 4). The technique is now well standardized and does not require detailed general description. Following resection of the coarctation, further trimming or tailoring of the aortic ends should be performed to provide the widest possible lumen at the point of anastomosis. Most commonly, a double-ended suture of fine silk or Dacron is started in the lateral posterior segment of the anastomosis and continued posteriorly as an over-and-over suture placed from the inside or as a continuous everting mattress suture. The other needle is used to bring the continuous suture around laterally for completion of the anastomosis.

In young children it may be desirable to perform at least the anterior portion of the suture line in an interrupted manner to allow for future growth. Great care must be exercised in holding the occluding vascular clamps and placing the suture line because of the extreme fragility of the aorta and adjacent intercostal arteries. End-to-end anastomosis was used for aortic reconstruction in 89 per cent of children in the first decade of life and in 63 per cent of patients between the ages of 10 and 20 years. Beyond the age of 20 years, resection and direct anastomosis was employed in a minority of patients in each age decade of life (Fig. 5).

Wedge Resection and Repair.—Occasionally, particularly favorable anatomic factors in young individuals with very short isthmic coarctations may

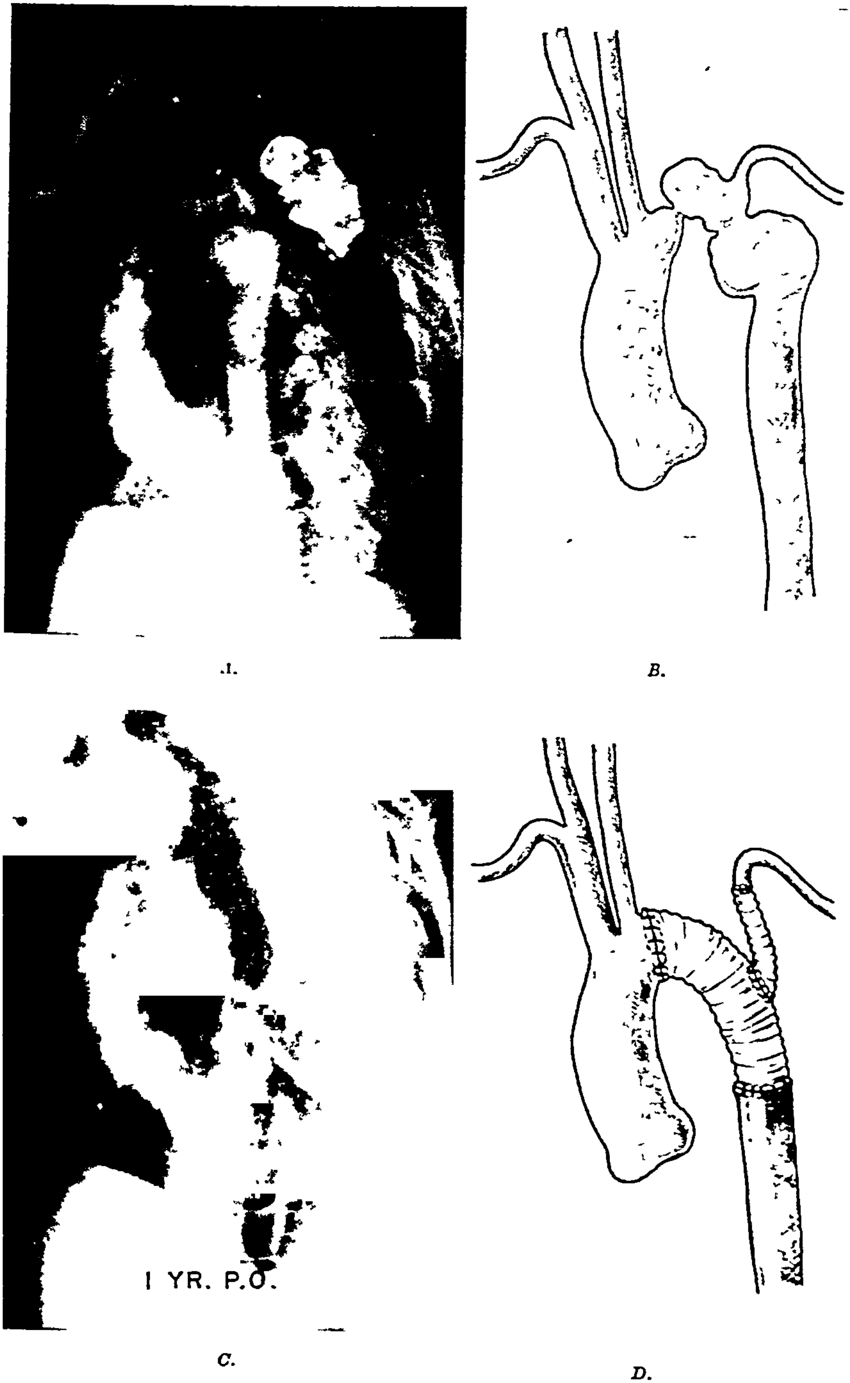
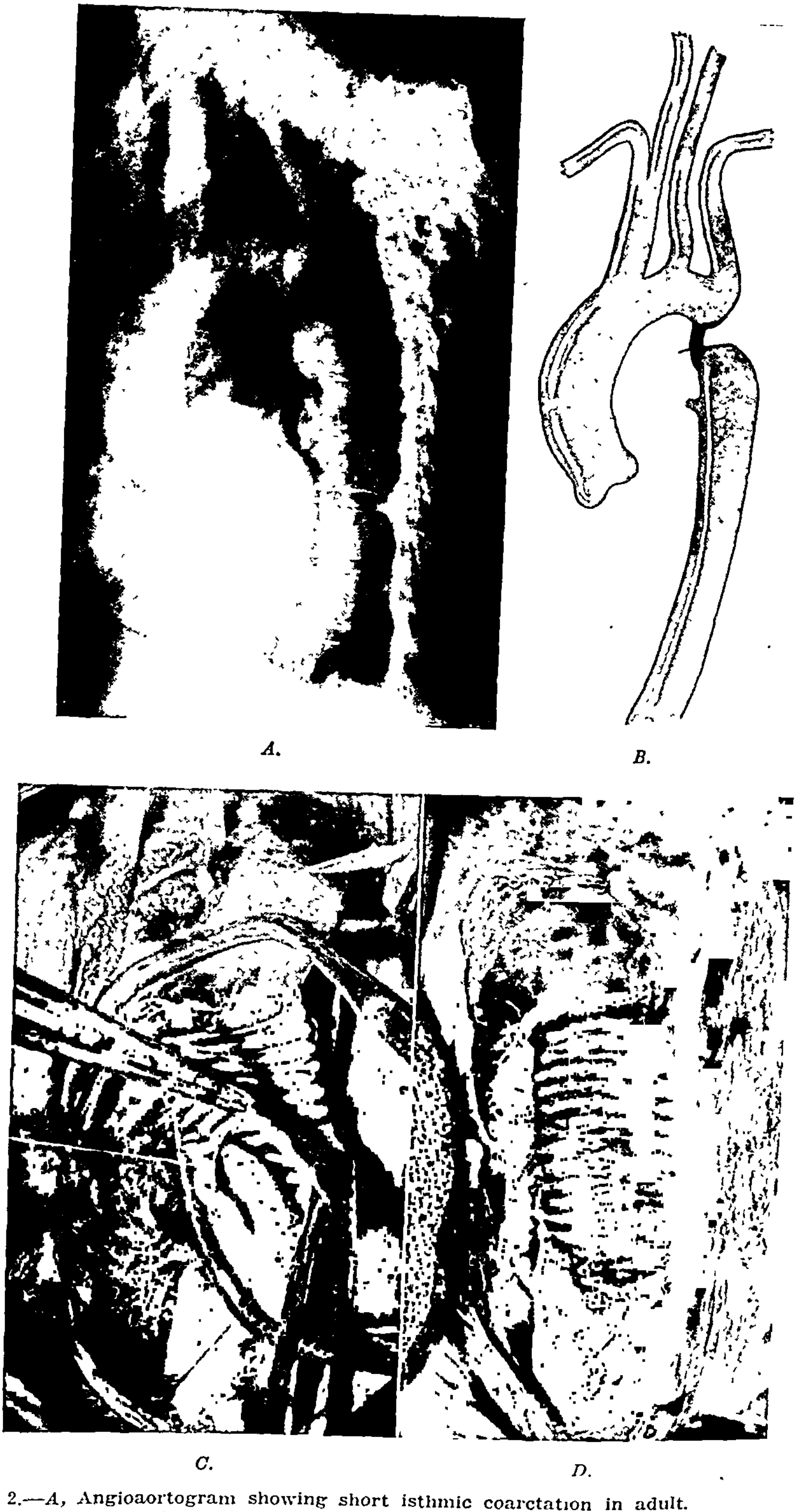


Fig 1.—*A*, Angioaortogram made before operation showing aneurysms associated with coarctation. Resected segment of aorta is superimposed.

B, Drawing which shows relation of aneurysms to coarctation and left subclavian artery.

C, Angioaortogram made after operation showing restoration of normal aortic lumen and contour.

D, Drawing which shows technique of aortic reconstruction.



A.

B.

C.

D.

Fig. 2.—*A*, Angioaortogram showing short isthmic coarctation in adult.

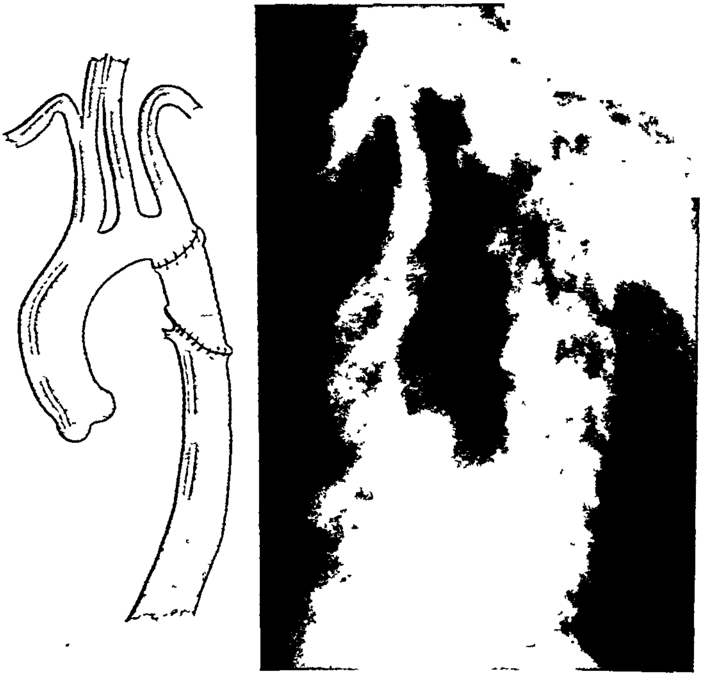
B, Drawing which shows location of coarctation.

C, Photograph made at operation showing placement of suture line for distal anastomosis between graft and aorta. Curved clamps have been applied in such a manner that wide anastomosis is possible after resection of coarctation.

D, Photograph made at operation showing functioning graft replacement of coarctation.

make wedge resection laterally with direct repair a satisfactory technical procedure. The suture repair is essentially similar to end-to-end anastomosis except that the posteromedial wall of the aorta in the stenotic area is not resected and forms one segment of the aortic wall opposite the suture line. Indications for application of this technique were uncommon in our experience as reflected by its use in only 3 per cent of 171 coarctations.

Resection and Graft Replacement.—End-to-end placement of graft to establish aortic continuity has had four general indications in this series: (1) long coarctations of the so-called infantile or preductile type, (2) coarctations involving the aortic arch with stenosis extending proximal to the subclavian artery, (3) subisthmic coarctations involving the middle and lower third of the descending thoracic or upper abdominal aorta, and (4) any type of coarctation in which local degenerative changes made direct anastomosis hazardous. During the past 4 years, Dacron grafts have been used with extraordinary success. Graft repair minimizes necessary dissection of the distal aortic segment since a suitably curved vascular clamp may be employed to control this segment and exclude the origin of the intercostal vessels. This approach reduces hazardous dissection about fragile and diseased second and third intercostal arteries (Fig. 6). Similarly, a conveniently curved vascular clamp may be applied proximally in such a manner as to exclude varying



E. *F.*

Fig. 2.—Cont'd. *E*, Drawing which shows graft replacement of coarctation. *F*, Angioaortogram made following resection and graft replacement of coarctation showing normal aortic lumen and contour.

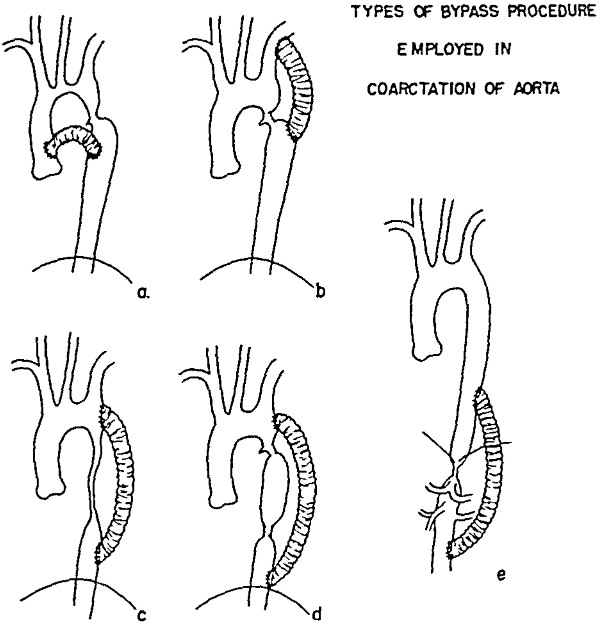
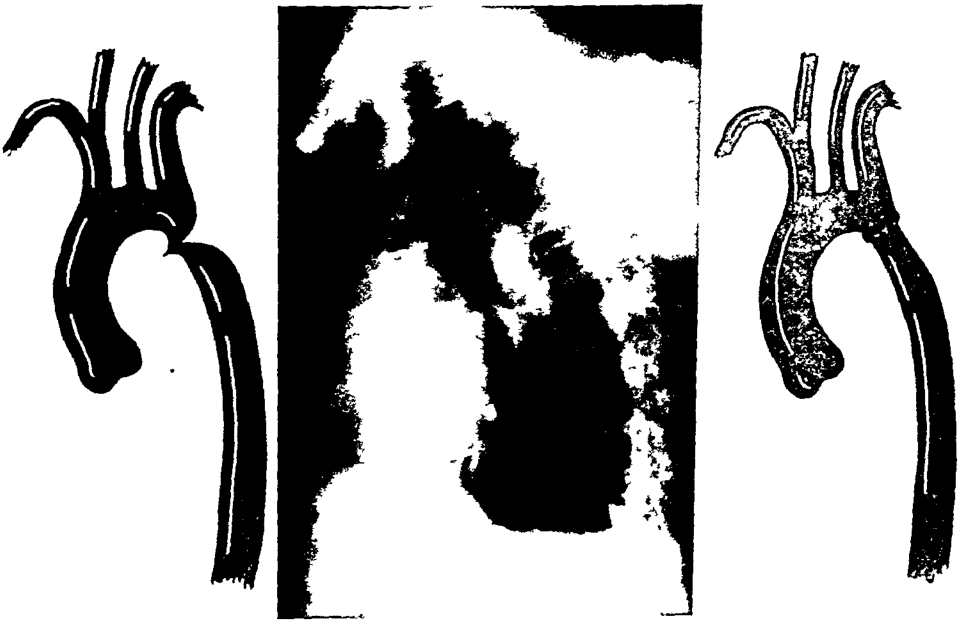


Fig 3 —Drawings which show types of bypass procedure employed in coarctation of aorta



A.

B

C

Fig 4 —A, Drawing which shows short isthmic type coarctation in young patient suitable for resection and end-to-end anastomosis

B, Angioaortogram made after resection and end-to-end anastomosis showing normal aortic lumen and contour.

C, Drawing which shows end-to-end anastomosis portions of the concave segment of the transverse aortic arch. Thus, by incising the aorta along its concave excluded wall for subsequent graft attachment, hypoplasia of the transverse aortic arch may satisfactorily be corrected. After selection and tailoring of a graft of suitable diameter, the proximal anastomosis is first completed using a continuous over-and-over suture of fine silk or Dacron. The graft is then cut to the appropriate length and obliquely tailored for distal anastomosis with the post-stenotic aortic segment. Just

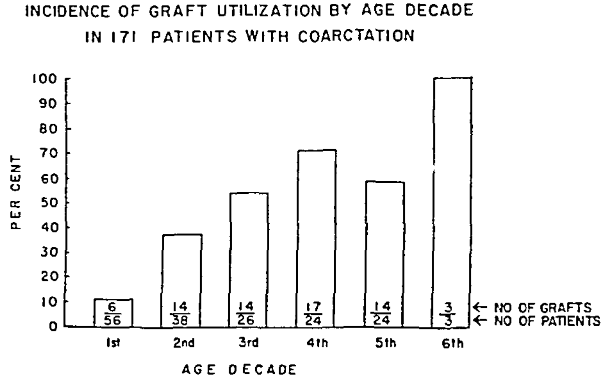


Fig. 5.—Graph which shows incidence of graft utilization by age decade.

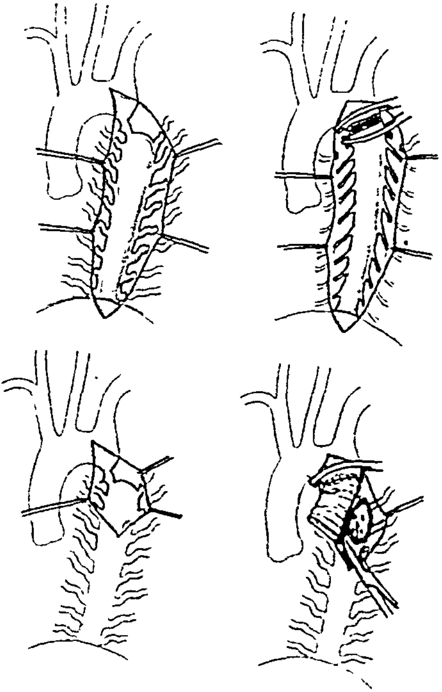


Fig. 6.—Drawings which compare extent of dissection usually necessary for resection and end-to-end anastomosis *(upper)* and resection with graft replacement *(lower)*.

before completion of the distal anastomosis, both proximal and distal occluding clamps should be momentarily released to flush the proximal and distal aortic segments. The distal clamp is removed first after completing the anastomosis This allows inspection of the anastomosis under lower arterial pressure and provides a few moments to place additional interrupted sutures if indicated. The proximal aortic clamp is very gradually released to minimize bleeding and avoid sudden reduction in arterial pressure.

When the coarctation (or associated degenerative changes) involve the arch and the left subclavian artery must be isolated, it is usually desirable to establish aortic continuity first. The subclavian artery can be subsequently connected using a small exclusion clamp on the convex curve of the graft to facilitate anastomosis, either directly or by means of a side arm extension.

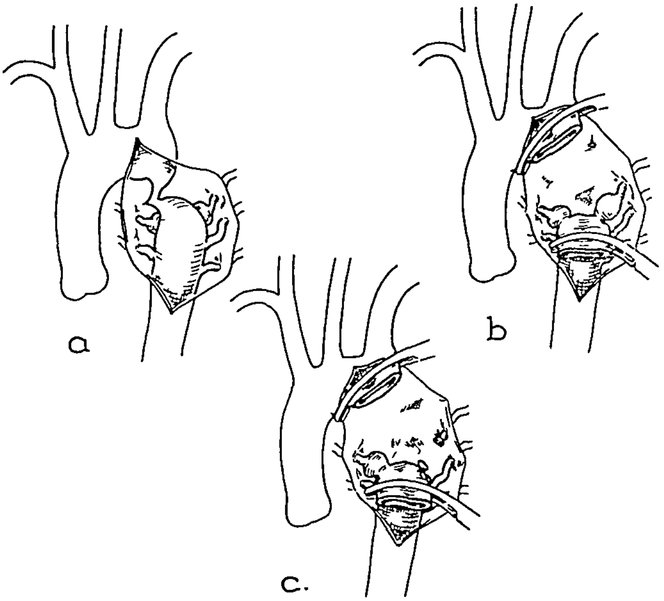
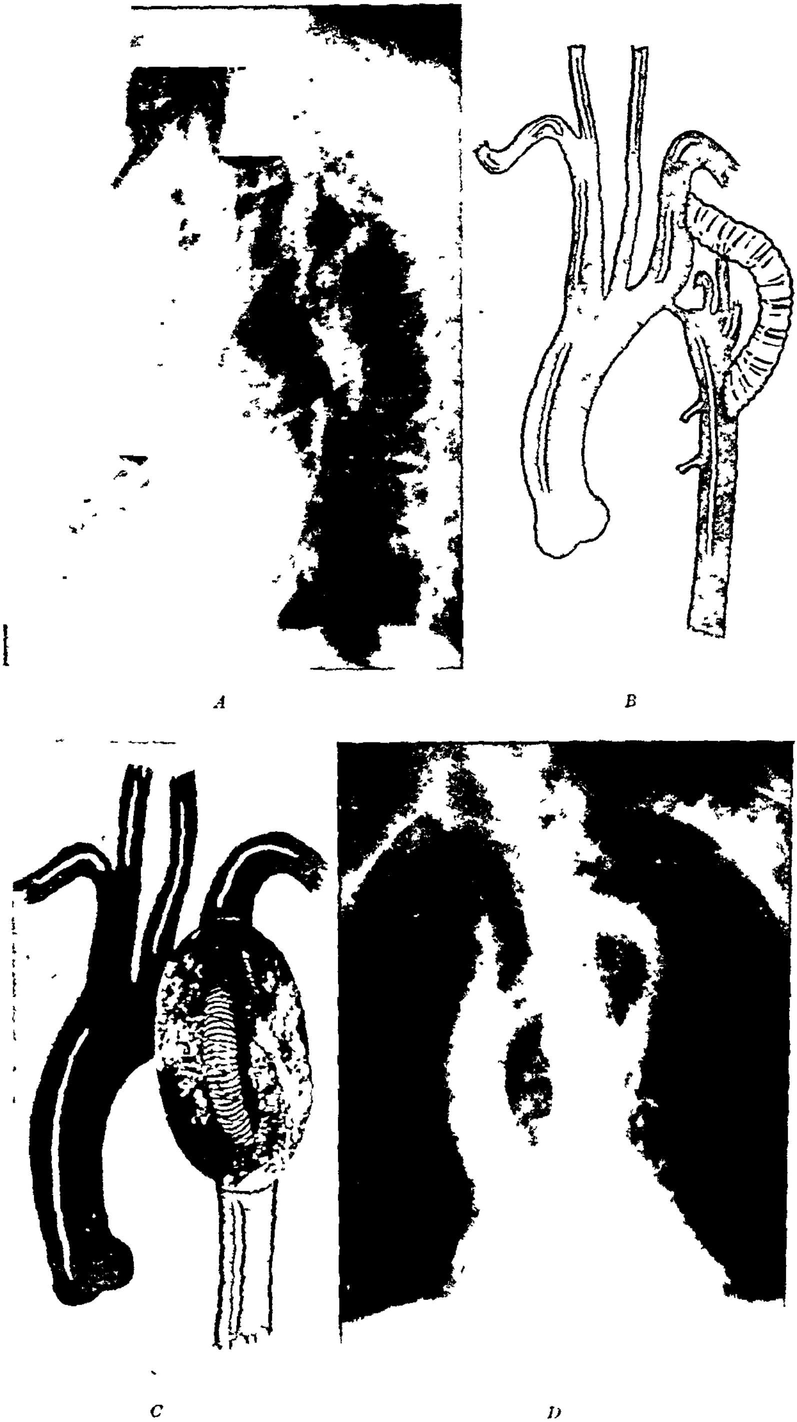


Fig 7 —Drawings which show technique of exposure for resection of intercostal artery aneurysms Coarctation initially exposed (*a*) and aorta cross-clamped and divided above coarctation (*b*) With distal aortic segment elevated, intercostal aneurysms are easily exposed for resection (*c*)

This approach reduces the period of aortic occlusion and provides attachment of the subclavian artery to the most desirable location on the graft, thus avoiding either tension or angulation.

Aneurysms of the upper intercostal arteries require resection for satisfactory surgical treatment. A technique which we have found of real merit in exposing and dissecting such intercostal arteries is application of occluding aortic clamps just above the coarctation followed by division of the aorta. Thus, with the distal aortic segment elevated, resection of aneurysmal intercostal arteries is greatly facilitated (Fig. 7)

Aortic Bypass.—The bypass principle is useful in certain unusual circumstances (Figs. 8 and 9). There are a number of general indications in



A B C D

Fig 8—1. Angioaortogram showing short isthmic coarctation in adult with coronary artery disease

B, Drawing which shows technique of bypass graft from left subclavian artery to aorta.
C, Drawing with superimposed operative photograph showing graft bypass.
D, Angioaortogram made after operation showing functioning bypass graft.

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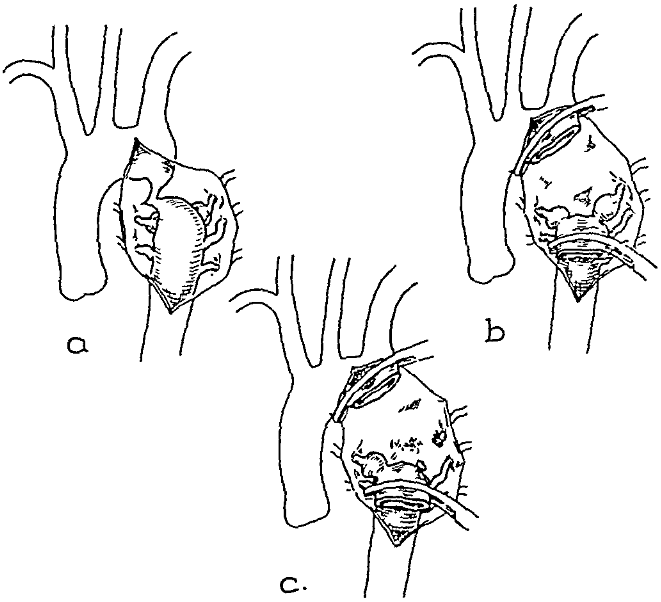

Fig. 7.—Drawings which show technique of exposure for resection of intercostal artery aneurysms. Coarctation initially exposed *(a)* and aorta cross-clamped and divided above coarctation *(b)*. With distal aortic segment elevated, intercostal aneurysms are easily exposed for resection *(c)*.

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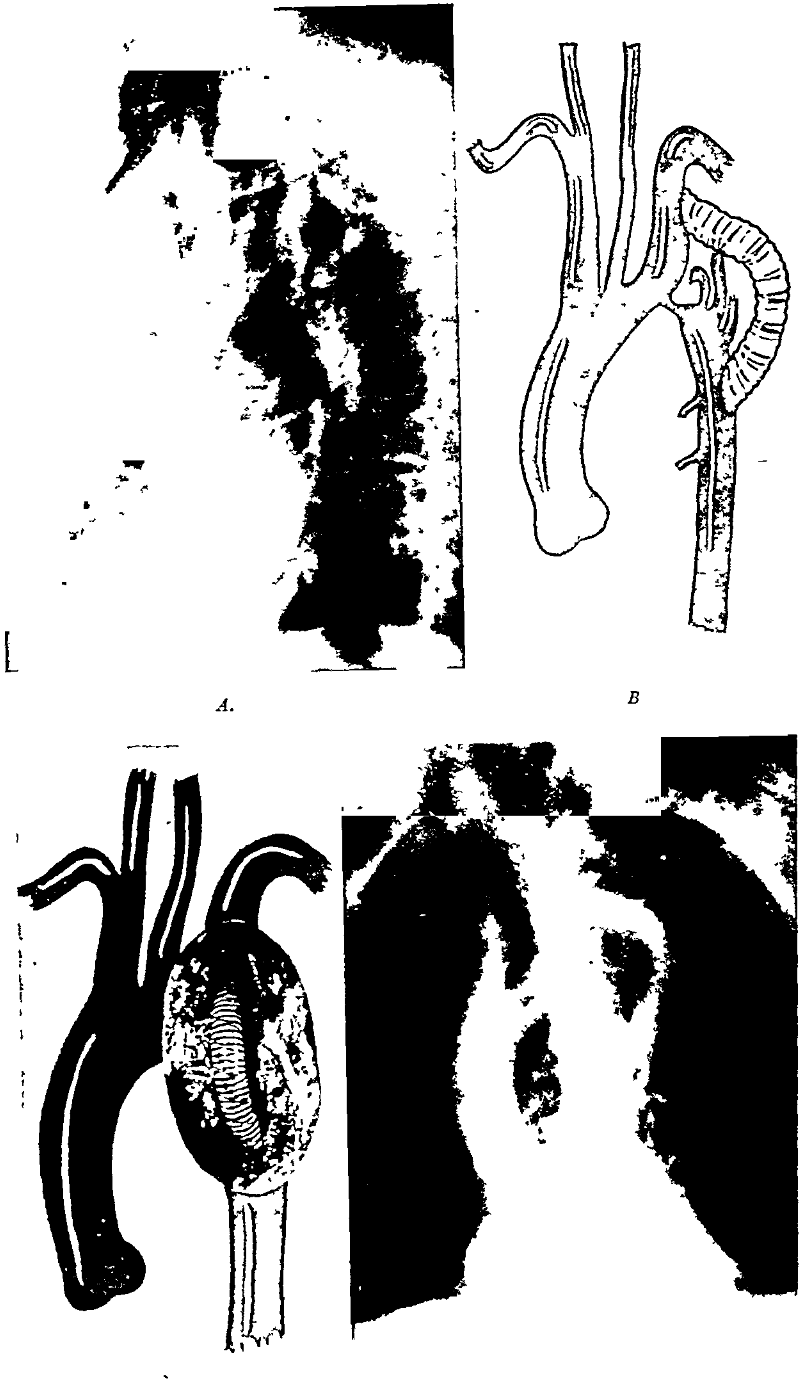

Fig. 8.—*A*, Angioaortogram showing short isthmic coarctation in adult with coronary artery disease.

B, Drawing which shows technique of bypass graft from left subclavian artery to aorta.

C, Drawing with superimposed operative photograph showing graft bypass.

D, Angioaortogram made after operation showing functioning bypass graft.

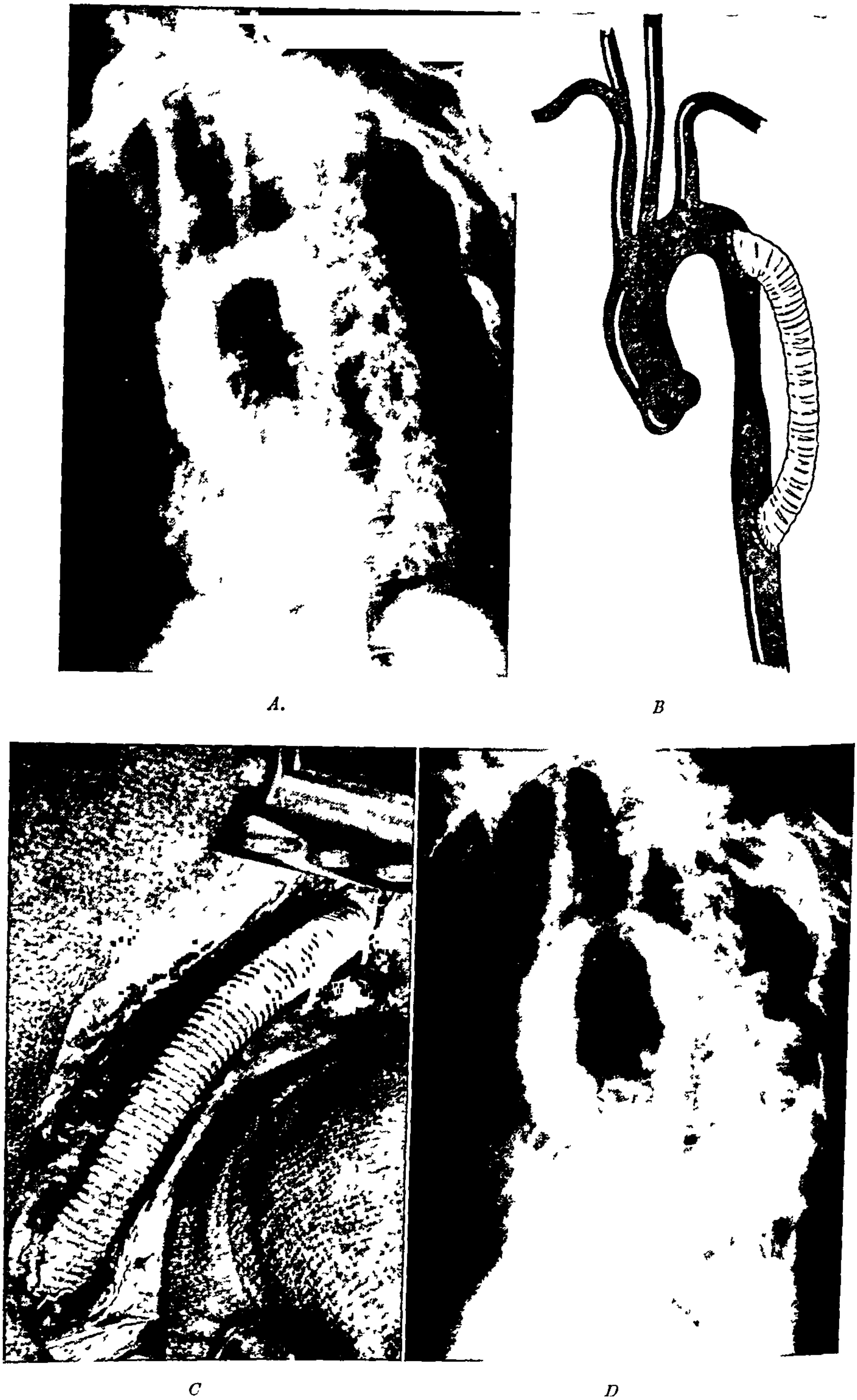

Fig 9.—*A,* Angioaortogram showing long area of obliterative process involving descending thoracic aorta

B, Drawing which shows location and extent of occlusive involvement and technique of graft bypass

C, Photograph made at operation showing bypass graft

D, Angioaortogram made after operation showing functioning bypass graft.

which application of this technique has appeared desirable: (1) situations in which resection of the coarctation may be hazardous, (2) poor-risk patients in whom this procedure facilitates expeditious surgical correction, (3) cases of long segmental involvement or multiple areas of stenosis, and (4) coarctations involving the lower thoracic and upper abdominal aorta. Appropriate exclusion clamps are applied to convenient segments of the aortic or subclavian wall proximally and the poststenotic aorta distally. With aortic blood flow essentially unaltered a linear incision can be made in the excluded segment for graft attachment. Proximal side-to-end anastomosis is completed first, followed by the distal end-to-side anastomosis to the aorta below the coarctation. Again flushing of the graft and gradual release of the proximal clamp is advantageous.

ANALYSIS OF CASES

During a period of 8 years, surgical correction of coarctation of the aorta was accomplished in 171 cases. The series consisted of 108 males (63 per cent) and 63 females (37 per cent). The age distribution was rather broad, extending from 19 children under the age of 1 year to 3 adults in the sixth decade. An analysis of age by decade has been compiled and reveals that almost half of these patients were over 20 years of age (Table I). Some of the clinical findings of particular interest are as follows. Hypertension in the brachiocephalic distribution was observed in 87 per cent of the cases. Neurologic alterations as a result of hypertension were seen in 25 per cent and ranged from relatively minor and reversible opthalmologic changes to hemiparesis. Cardiac decompensation had occurred in 36 per cent of the cases. Roentgenographic evidence of rib erosion or notching associated with enlarged intercostal arteries was seen in 61 per cent of the 171 cases. Accompanying patent ductus arteriosus was present in 44 cases (26 per cent).

TABLE I. ANALYSIS OF AGE IN 171 CASES OF SURGICALLY TREATED COARCTATION OF THE AORTA (NUMBER OF CASES IN EACH AGE DECADE)

	NUMBER	PER CENT
1st decade	56	33
2nd decade	38	22
3rd decade	26	15
4th decade	24	14
5th decade	24	14
6th decade	3	2
Totals	171	100

The anatomic location of the coarctation was in the region of the aortic isthmus in 152 cases (Table II). In 10 cases the stenosis began proximal to the left subclavian artery and involved the aortic arch. In 9 instances the coarctation presented itself in a subisthmic location, with 5 located in the middle and lower thirds of the descending thoracic aorta and 4 in the upper abdominal aorta. Not included in this series are an additional 15 cases with occlusive processes produced by various etiologic factors with occlusion of the abdominal aorta between the renal and inferior mesenteric arteries.[15] Aortographic visualization to show level and extent of the coarctation seemed justified only in a minority of patients. This study is essential in patients with clinical features suggesting coarctation in unusual locations and in older adults to delineate associated degenerative changes such as aneurysm. Reduced blood pressure in the left arm suggests involvement of the transverse aortic arch. Classical findings that suggest subisthmic coarctation involving the lower thoracic or upper abdominal aorta are absence of murmur or, when present, located at a lower level; absence of notched ribs or, when present, notching of only the lowest ribs; absence of latissimus pulsation and an increased propensity for lower extremity claudication.

TABLE II. COARCTATION OF AORTA (ANATOMIC LOCATION)

LOCATION	NUMBER	PER CENT
Isthmus	152	89
Arch	10	6
Subisthmus		
Descending thoracic aorta	5	3
Upper abdominal aorta	4	2
Totals	171	100

For purposes of analysis the type of surgical repair has been divided into four general categories. These divisions, together with the numbers in each, are as follows: end-to-end anastomosis 98 cases (58 per cent), wedge excision and suture 5 cases (3 per cent), resection and graft replacement 60 cases (35 per cent), and bypass with a graft 8 cases (4 per cent). The high incidence of graft application (68 cases) reflects the relatively large number of patients in the third, fourth, and fifth decades of life with attendant local degenerative changes in the aorta. In eight instances the origin of the left subclavian artery was resected which required suture of this vessel to the side of the graft. Bypass graft without resection was used in one coarctation involving the transverse aortic arch, in 2 poor-risk adults with isthmic coarctation, in two subisthmic coarctations, and in 3 patients with upper abdominal coarctation.

There were eight operative deaths in this series of 171 cases for a mortality rate of 4.6 per cent. Two children with coarctation of the upper abdominal aorta and associated atresia of the renal arteries died of sequelae arising from renal failure and 1 of these patients had endocardial fibroclastosis. Two infants died with pulmonary insufficiency associated with ventricular septal defects. Delayed hemorrhage from rupture or tear of the aorta near the suture line caused one death and coronary occlusion was fatal in one other case. Transfusion reaction and mesenteric arteritis accounted for two deaths, respectively. Follow-up studies revealed an additional four deaths 6 weeks to 1 year after operation. Two were the result of coronary occlusion, one was due to infection in the suture line of an end-to-end anastomosis, and one resulted from unknown causes.

DISCUSSION

Experience in this series of 171 coarctations of the aorta appears unusual because it includes a high percentage of challenging surgical problems in patients who may be placed in the following groups—infants, patients over 30 years of age, and those with anatomic variants.[2, 11] There were 19 desperately ill infants under 1 year of age with intractable congestive heart failure and frequently associated cardiovascular malformations. Only two deaths occurred in this infant group for a mortality rate of 10 per cent and both deaths resulted from pulmonary insufficiency associated with large ventricular septal defects. Another group of patients presented unusual anatomic problems requiring a variety of far from standard surgical techniques for operative correction (Fig. 10). Two deaths in this group resulted from the anatomically and technically insoluble problem of diffuse bilateral renal artery hypoplasia. Finally, one of the most significant features in this series of surgically corrected coarctations was the high incidence of older adults. Forty-five per cent of patients were in the third to sixth decades of life. Two late deaths occurring in this group were due to coronary occlusion 6 weeks to 1 year after operation. Nonetheless the operative mortality of 4.6 per cent compares favorably with reports by others.[2, 11] Although elimination of these various challenging groups of coarctations could provide us with an extremely low mortality rate, the gratifying salvage of most such patients has continually reduced the number of patients in whom operative correction appeared contraindicated.

Our experience with the Dacron graft during the past 5 years has proved this material eminently satisfactory, not only for technical ease in handling during aortic reconstruction but, of more importance, for its long-term reliability.[7] It has maintained its tensile strength and has demonstrated no instances of late degenerative complications, such as aneurysm formation which is seen occasionally with homografts and nylon grafts. Application of graft reconstruction for aortic coarctation provides an almost limitless number of variations in surgical technique to meet individual problems. In most adults, reconstruction with a graft offers replacemment of the coarctation with an aorta of normal size and shape, thus reconstituting normal hemodynamics (Fig. 11). Probably the most significant factor in the high rate of graft application in our adult patients has been associated reduction in operative hazards with its employment. Dissection about the aorta may be greatly minimized and fragile intercostal arteries avoided. After applying suitably curved clamps to exclude the area of coarctation, the process can be removed together with diseased segments of the aortic wall and the aortic segments can be tailored obliquely to allow placement of a graft commensurate with aortic size. A secondary benefit derived from this approach is the technical facility with which the procedure can be accomplished with significantly reduced operative time. There appears now no justification for withholding use of a graft in adults if its employment will improve aortic reconstruction or provide a wider margin of safety. We are now so confident of the long-term results with

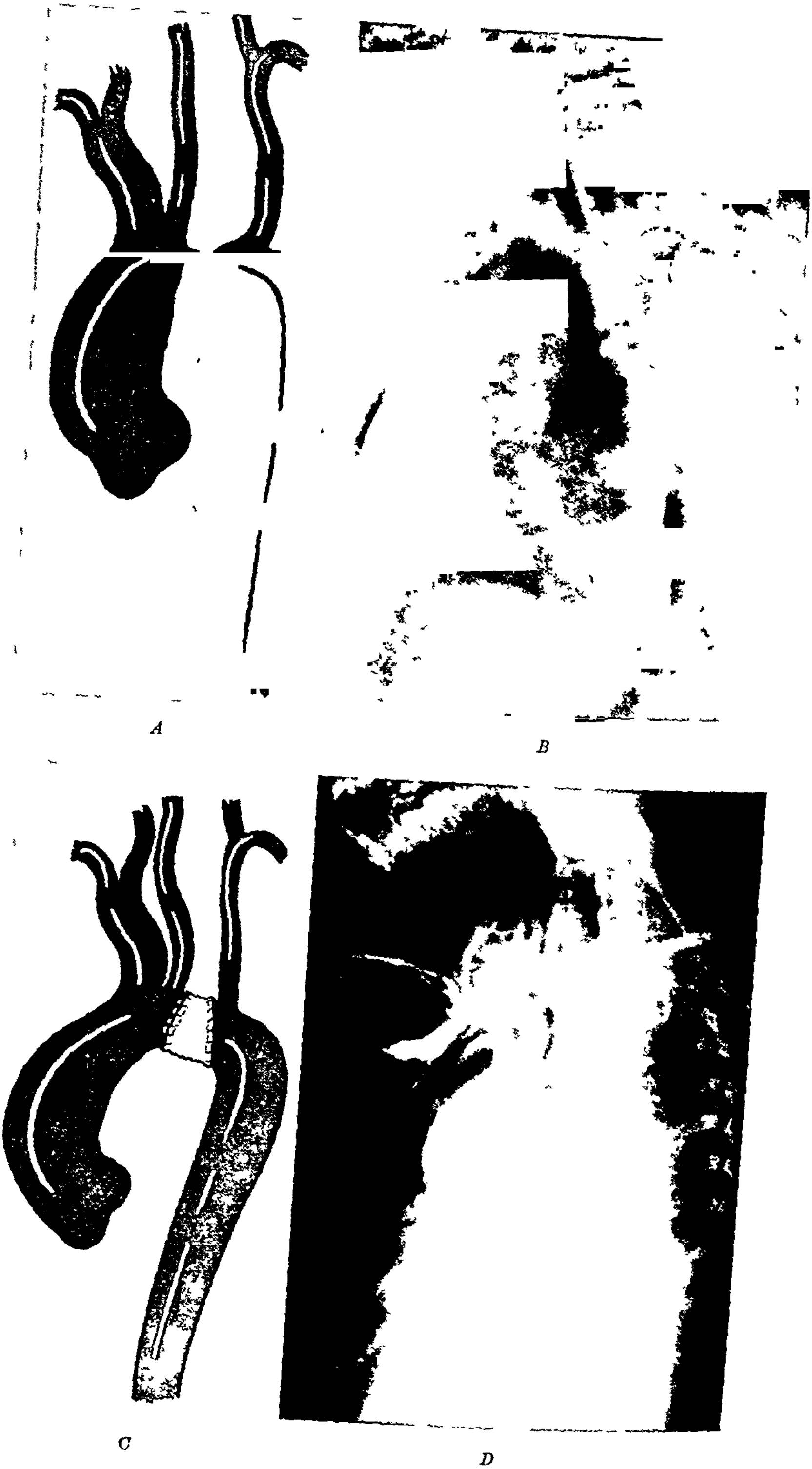

Fig. 10—*A*, Drawing which shows unusual location of coarctation in transverse aortic arch
B, Angioaortogram which shows coarctation between left carotid and subclavian arteries
C, Drawing which shows technique of aortic resection and reconstruction with a graft.
D, Angioaortogram made after operation which shows reconstructed aortic arch.

the Dacron graft that we have little reluctance for its use even in children, when indication appears justified. During the past 3 years, incidence of graft utilization has remained at a high level exceeding 50 per cent application in each year (Fig. 12).

SUMMARY

Previous limitations placed upon selection of patients with coarctation for operation based upon age, length of the aortic occlusion, and presence of

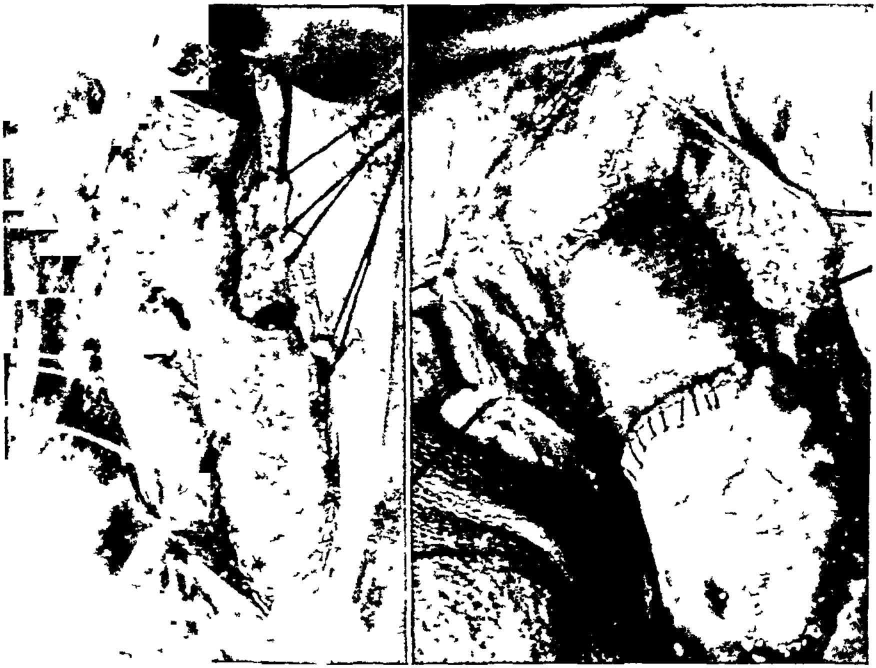

Fig. 11.—A, Photograph made at operation showing elongated isthmic coarctation. B, Photograph made at operation which shows graft replacement after resection of coarctation and adjacent hypoplastic aorta with reconstructed aorta of normal size and contour.

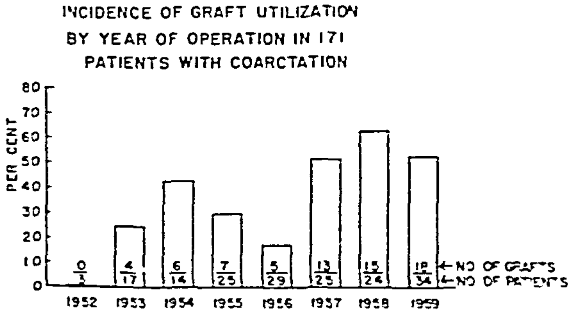

Fig. 12.—Graph which shows incidence of graft utilization by year of operation in 171 patients with coarctation.

associated pathologic lesions, such as atheromatous or aneurysmal disease, have been considerably altered by new concepts of surgical repair.

The primary objective of surgical treatment for coarctation is concerned with the hemodynamic disturbance produced by the occlusive process. This objective may be achieved in most forms of the disorder by resection of the coarcted segment with end-to-end anastomosis or with graft replacement. In those associated with aneurysmal formation, extirpation of the lesion is essential. In occasional instances the bypass graft may be the treatment of choice.

An analysis of 171 surgically treated patients with coarctation is presented in which newer surgical techniques have been applied to meet a number of challenging problems.

REFERENCES

1. Broden, B., and Karnell, J.: Coarctation of the Aorta; Aortographic Studies Before and After Operation, Acta radiol., Stockholm 50: 1-61, 1958.
2. Burford, T. H., Ferguson, T. B., Goldring, D., and Behrer, M. R.: Coarctation of the Aorta in Infants: A Clinical and Experimental Study, J. THORACIC SURG. 39: 47, 1960.
3. Clagett, O. T., Kirklin, J. W., and Edwards, J. E.: Anatomic Variations and Pathologic Changes in Coarctation of the Aorta; A Study of 124 Cases, Surg. Gynec. & Obst. 98: 103, 1954.
4. Cooley, D. A., and De Bakey, M. E.: Resection of the Thoracic Aorta With Replacement by Homograft for Aneurysms and Constrictive Lesions, J. THORACIC SURG. 29: 66, 1955; correction 29: 216, 1955.
5. Crafoord, C., and Nylin, G.: Congenital Coarctation of Aorta and Its Surgical Treatment, J. THORACIC SURG. 14: 347, 1945.
6. De Bakey, M. E.: Presidential Address: Changing Concepts in Thoracic Vascular Surgery, J. THORACIC SURG. 38: 145, 1959.
7. De Bakey, M. E., Cooley, D. A., Crawford, E. S., and Morris, G. C., Jr.: Clinical Application of a New Flexible Knitted Dacron Arterial Substitute, Am. Surgeon 24: 862, 1958.
8. Edwards, J. E., Christensen, N. A., Clagett, O. T., and McDonald, J. R.: Pathologic Considerations in Coarctation of Aorta, Proc. Staff Meet. Mayo Clin. 23: 324, 1948.
9. Ellis, F. H., Jr., and Clagett, O. T.: Coarctation of the Aorta Proximal to the Left Subclavian Artery: Experience With Six Surgical Cases, Ann. Surg. 146: 145, 1957.
10. Gross, R. E., and Hufnagel, C. A.: Coarctation of the Aorta; Experimental Studies Regarding Its Surgical Correction, New England J. Med. 233: 287, 1945.
11. Groves, L. K., and Effler, D. B.: Problems in the Management of Coarctation of the Aorta, J. THORACIC SURG. 39: 60, 1960.
12. Gupta, T. C., and Wiggers, C. J.: Basic Hemodynamic Changes Produced by Aortic Coarctation of Different Degrees, Circulation 3: 17, 1951.
13. Hallenbeck, G. A., Wood, E. H., Burchell, H. B., and Clagett, O. T.: Coarctation of the Aorta; Relationship of Clinical Results to Cardiovascular Dynamics Studied Before, During, and After Surgical Treatment, Surg. Gynec. & Obst. 92: 75, 1951.
14. Kirkendall, W. M., Culbertson, J. W., and Eckstein, J. W.: Renal Hemodynamics in Patients With Coarctation of the Aorta, J. Lab. & Clin. Med. 53: 6, 1959.
15. Morris, G. C., Jr., De Bakey, M. E., Cooley, D. A., and Crawford, E. S.: Subisthmic Aortic Stenosis and Occlusive Disease, A. M. A. Arch. Surg. 80: 87, 1960.
16. Nicks, R.: A Surgical Study of Coarctation of the Aorta, Brit. Heart J. 20: 351, 1958.
17. Niedner, F. J.: Treatment of Aortic Isthmus Stenosis; Procedure in Patients With Advanced Changes of the Aortic Wall, Arch. klin. Chir. 287: 438, 1957.
18. Oeconomos, N.: Dacron Prosthesis for Coarctation of Aorta With Aneurysm; Report of a Case in a Pregnant Woman, A. M. A. Arch. Surg. 77: 181, 1958.
19. Scott, H. W., Jr., Collins, H. A., Langa, A. M., and Olsen, N. S.: Additional Observations Concerning the Physiology of the Hypertension Associated With Experimental Coarctation of the Aorta, Surgery 36: 445, 1954.
20. Steinburg, I., and Sammons, B. P.: Aneurysmal Dilation of the Aortic Sinuses in Coarctation of the Aorta; Report of Two New Cases and Review of the Literature, Ann. Int. Med. 49: 922, 1958.

21. Temesvári, A., and Árvay, A.: Some Clinical and Pathologic Aspects of Coarctation of the Aorta and Aortic Arch Syndrome, J. THORACIC SURG. 36: 247, 1958.
22. Wright, J. L., Burchell, H. B., Wood, E. H., Hines, E. A., Jr., and Clagett, O. T.: Hemodynamic and Clinical Appraisal of Coarctation Four to Seven Years After Resection and End-to-End Anastomosis of the Aorta, Circulation 14: 806, 1956.

DISCUSSION

DR. SAMUEL R. SCHUSTER, Boston, Mass.—This paper is especially interesting to us at the Children's Hospital in Boston, because we are just reviewing our own series of 505 coarctations which we have resected in the past 15 years.

In these cases we try to do a direct end-to-end suture. In 70 cases we inserted a graft. It is our belief that a graft should be inserted whenever necessary, but an end-to-end anastomosis is considered mandatory whenever possible.

We have attempted to do this by carrying out a more adequate mobilization of the aorta than was demonstrated in the paper today; a great deal of mobility can be gained by carrying the dissection of the aorta considerably farther down toward the diaphragm.

There has been no failure at the suture line, except in 2 patients with subacute bacterial endocarditis.

We have used homografts in all patients requiring grafting and have seen a fair amount of calcification in some of these homografts. However, we have not seen any aneurysmal distention of the homografts. We have not seen any occlusion of the homografts and, for the present, we see no reason to change to a prosthetic material.

We have performed one operation for coarctation of the abdominal aorta by using a homograft bypass, the bypass extending from above the diaphragm to below the renal vessels, with a good result.

DR. FRANCIS S. GERBASI, Detroit, Mich.—I rise to emphasize that coarctations of the aorta can occur elsewhere than in the thoracic aorta, and I think that we can make this diagnosis if we very carefully examine the entire chest and abdomen for bruits and pulsations.

I didn't do this 4 years ago, when I operated on a young girl 11 years old. I was sure I was going to find a coarctation in the upper thoracic aorta. I did a thoracotomy, and it wasn't there. I put my finger down along the aorta, and, sure enough, it was in the abdomen. We were using homografts at that time, and as I didn't have a graft long enough to do anything, I closed the chest.

A week later I did a retrograde aortogram [slide], which showed she had a coarctation of the abdominal aorta right in the area of the celiac axis. Here is the splenic artery [indicating], and there is the hepatic.

Two weeks later, through a thoracoabdominal incision, I explored the entire abdominal and lower thoracic aorta. The stenotic area involved the aorta at the site where the celiac axis came off. I was very hesitant about doing an end-to end anastomosis there because the celiac artery itself was very small, and I was sure it would thrombose if it were anastomosed to the side of the graft. I did what I thought was the next best thing—a bypass around the coarctation.

[Slide] It has now been 4 years since the operation. Before her operation she had a brachial pressure of 200/120 mm. Hg. It is now 110/70 mm. Hg, and she is asymptomatic.

DR. FRANK C. SPENCER, Baltimore, Md.—I rise to mention the use of the bypass principle in 2 unusual cases of long coarctation in the aortic arch. The atretic area began distal to the innominate artery, was 7 to 10 cm. in length, and involved the origins of the left carotid and subclavian arteries. Both patients were children operated upon at the Walter Reed Army Hospital; one was 2 and one was 12 years of age. In each child it was obvious on physical examination that the coarctation extended far proximally because the right carotid pulse was unusually prominent and the left carotid pulse absent; on angiography it could be seen that the coarctation began just distal to the origin of the innominate artery. The younger child also had some cyanosis of the lower extremities.

An anterior incision in the fourth intercostal space was used in order to have access to the ascending aorta. With the area exposed it was easily possible to insert a Dacron graft proximally into the aorta at the origin of the innominate artery and distally into the side of the descending aorta. A large ductus was also divided in the younger patient. Convalescence in both patients was uneventful.

DR. MORRIS (Closing).—I am indebted to the discussers for their interesting remarks.

In relation to Dr. Schuster's comments, I would certainly imagine that a preponderance of his cases were in children, and we certainly agree that end-to-end anastomosis is the treatment of choice. One objective in this presentation was to emphasize other techniques for challenging problems commonly seen in adults and in unusual anatomic types of coarctations.

With reference to abdominal coarctation, Dr. Gerbasi, we have had this problem also. We have had patients in our series with two separate areas of coarctation. In one, we initially missed the second coarctation and a second operation was necessary, but in the second case we were able to diagnose both lesions before operation and thus repair both concomitantly.

We also had some interesting cases such as Dr. Spencer described. In one particular case there was coarctation involving all of the transverse aortic arch, with extreme calcification of the aortic wall. We found two soft spots, one in the ascending aorta and one in the descending, and simply used a bypass graft directly across the arch.

FIVE-YEAR FOLLOW-UP STUDY OF CLOSED MITRAL VALVULOTOMY

J. Gordon Scannell, M.D., John F. Burke, M.D. (by invitation), Farrokh Saidi, M.D. (by invitation), and John D. Turner, M.D. (by invitation), Boston, Mass.

The application of new techniques to operations on the mitral valve makes it imperative to review the long-term results of closed mitral valvulotomy. It is particularly important to do this in order to provide a rational basis for open operation as an initial procedure in mitral stenosis.

One hundred consecutive patients who *survived* mitral valvulotomy at the Massachusetts General Hospital between June 1952 and January 1955 form the basis of this report. Seven patients who died of operation define the operative mortality during this period, but have been excluded from this follow-up study which is concerned with long-term results of operation. Five years after operation is taken as the end point of the study for each patient but information beyond that time is included whenever relevant. Information adequate to permit an intelligent evaluation at 5 years has been obtained for the entire series of 100 patients. Follow-up data in terms of an office or clinic examination by ourselves or a member of our own medical staff are available in 76. In 15, detailed clinical information has been supplied by the patient's physician in response to a personal request for information on the part of the authors, the remaining 9 patients have been examined in cardiac clinics of affiliated hospitals.

Since the series begins in June 1952, the first 17 patients undergoing mitral valvulotomy at this hospital have been excluded. This has been done in order to standardize the clinical material by eliminating the learning curve of the early cases so far as possible. It is interesting to note that of the first 17 patients, 3 have come to reoperation.

Without wishing to become involved in semantics, we use the term mitral valvulotomy as a convenient one to describe forcible dilatation by the index finger of a stenotic mitral valve with resulting split of the fused commissures. In the series here reported, if an adequate split of the commissures did not occur as a result of digital pressure, an attempt was made to cut the fused commissures with a knife or an Olivekrona pituitary scissors, while palpating

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From the General Surgical Services and Cardiac Research Laboratory, Massachusetts General Hospital, Boston, Mass.

Read at the Fortieth Annual Meeting of The American Association for Thoracic Surgery at Miami Beach, Fla., May 11-13, 1960 the valve (15 of the entire series). At present, we prefer to use a mechanical dilator of the type advocated by Tubbs and Logan.[1]

In attempting to evaluate operative results, we have encountered the problem which troubles almost every group that reports the results of surgery for acquired valvular disease; namely, dissatisfaction with existing classifications and categories. We have, therefore, taken the usual course and set definitions which seem most applicable to the clinical material at hand.

In the preoperative evaluation we have recognized two groups of patients.

GROUP 1.—Individuals moderately to moderately severely incapacitated by their disease, of whom there were 74.

GROUP 2.—The severely incapacitated, of whom there were 26.

In general, these groups conform to American Heart Association classifications III and IV, respectively. The categories are intended to characterize the severity of disease, not the magnitude of operative risk which is an overworked and remarkably subjective term.

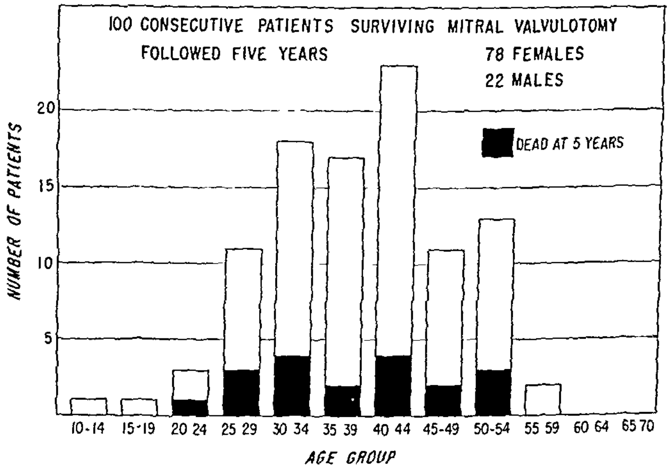


Fig. 1.—Age distribution of 100 patients surviving mitral valvulotomy, June 1952–January 1955.

In the postoperative evaluation of results, we have used the following scale of values.

1. The result is considered *excellent* if the patient is making no significant concessions to his disease, is free of symptoms under all reasonable conditions, tolerates periods of infection and stress (including pregnancy) well, and does not require salt restriction and cardiac medications. (An exception is the use of digitalis to control heart rate in the patient with atrial fibrillation.) Although such patients are generally under medical supervision, both the patient and the doctor are enthusiastic about the result.

2. The result is considered *good* if the patient is able to discharge his household or economic responsibilities without serious limitation, and requires only moderately strict medical supervision under conditions of physical stress or intercurrent infection. Both patient and physician are well satisfied with progress.

3. The result is adjudged *fair* if the patient is improved over his preoperative status, but still mildly or moderately incapacitated; requires careful medical supervision, restriction of salt intake, and occasional diuretics. Such patients usually are more enthusiastic about the result than the facts appear to justify.

4. The result is considered *poor* if the patient's condition is about the same as his preoperative status or worse.

5. Finally, *dead* is considered a category of result, irrespective of cause. In the present series, of 19 patients who died at or before 5 years, 11 died of congestive failure, 4 died of bacterial endocarditis, 1 each of cerebral embolus (at 4 mo.), pulmonary embolus (at 1 mo.), alcoholic cirrhosis, and sudden arrhythmia (patient up to that time [4 yr.] having done well).

The age distribution of the patients in this report is shown in Fig. 1. In general, it conforms to reported series elsewhere. Of greater importance, as will appear later under consideration of results, is the sex distribution. There were 78 females and 22 males. Calcification of the valve was found in only 15 per cent of the former, 55 per cent of the latter.

CLINICAL RESULTS

Of 100 consecutive patients who survived mitral valvulotomy, there were 81 alive 5 years after operation. (Five have since died.) Of these, 33 were rated as having excellent results and 28 good; to make a total of 61 unequivocally satisfactory results in terms of the initial operation. The results in 9 patients were considered fair and poor in 11 at 5 years. Of the latter group, 5 had undergone reoperation and survived, but in terms of the inital operation were considered to have poor results. Of the 19 patients who survived the initial operation, but who died within 5 years from causes enumerated above, 3 had undergone reoperation.

The 5-year results are presented graphically in Fig. 2. In addition, the results at yearly intervals are indicated. Thus, at 1 year, 78 patients were classified as good to excellent. At 2 years, 75 were so rated; at 3 years, 72; at 4 years, 67; and at 5 years, 61. The rather sharp drop of 23 per cent in the first year to 77 good to excellent results, with only a gradual decline of approximately 5 per cent per year thereafter, supports the clinical impression that the poor results generally become obvious within the first year—a phenomenon that is not surprising. After the first year there appears to be a steady attrition rate of about 5 per cent per year for the group as a whole. However, on an individual basis, if deterioration occurs, there is usually a rather obvious and sharp break in compensation. In our entire experience with reoperation for mitral stenosis, which now includes 8 closed and 18 open reoperations, the average interval between first and second operations was nearly 4 years.

It is extraordinarily difficult to find adequate controls against which to measure an operative series of patients with mitral stenosis. In Fig. 3 we have chosen to compare, in terms of survival, this group of 100 patients with

25 patients of so-called grade 3, and presumably comparable, severity, recently reported by Rowe, Bland, Sprague, and White.[2] By their definition, grade 3 means "moderate to moderately severe symptoms or one or more of the major complications (for example, embolism or endocarditis)." Since many of the patients of the present operative series were, in fact, under the care of the three senior authors of that follow-up study, and they had concurred in the indications for operation in the present series, it appears reasonable to use their grade 3 patients as "controls." It is recognized, of course, that their patients were treated in the "pre-surgical era" and hence were not strictly a "control" group. Their 5-year survival rate for "grade 3" was 27 per cent as opposed to 81 per cent for the present series.

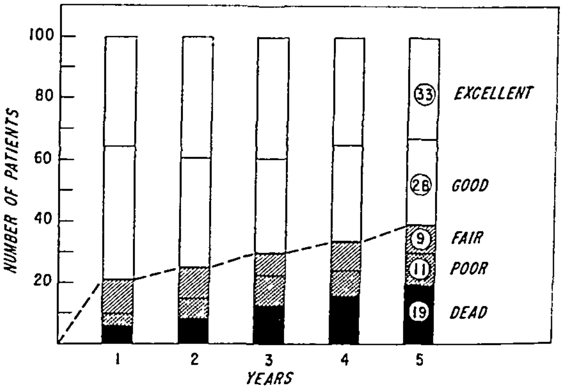
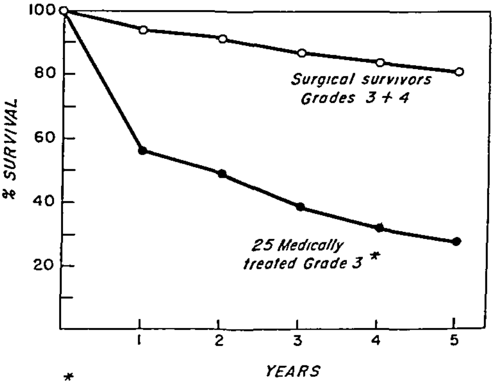


Fig. 2.—Clinical results (100 consecutive patients) at 5 years after operation, and at yearly intervals up to that time. See text for scale of values.



* from Rowe, Bland, Sprague, White, 1959

Fig. 3.—Comparison of survival rates in 100 consecutive patients with mitral stenosis treated surgically and medically.

In Fig. 4 we have compared the 5-year results in patients severely incapacitated prior to operation with individuals moderately to moderately severely incapacitated. Of the 26 severely incapacitated, 50 per cent were rated good to excellent at 5 years, 29 per cent were fair to poor, and 31 per cent were dead. Of 74 patients less severely limited, 65 per cent were considered good to excellent, 20 per cent fair to poor, and 15 per cent were dead.

In Fig. 5 we have grouped results in terms of isolated factors at the time the patient came to operation in order to determine their bearing on long-term results Thus, of 22 males, in only 36 per cent was the result adjudged good to excellent at 5 years, whereas of 78 females, 69 per cent were so rated. Of 24 patients noted to have significant calcification of the valve at operation (and this correlated only fairly well with pre-operative radiologic findings) only 29 per cent were doing well (that is, good to excellent) at 5 years, while

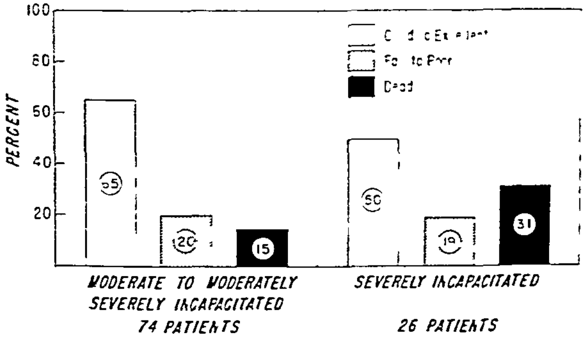


Fig 4—Clinical results at 5 years in 100 consecutive patients moderately and severely incapacitated at time of operation

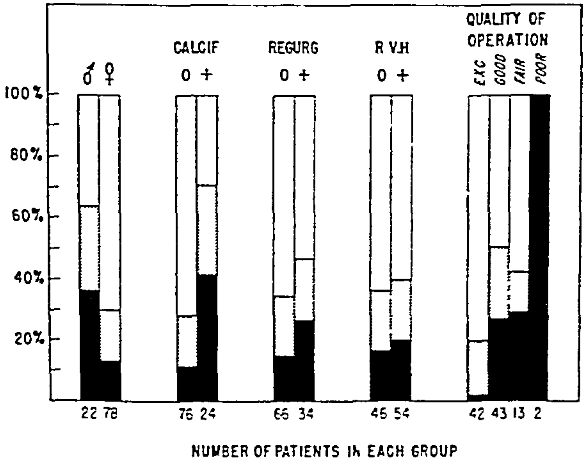


Fig 5—Clinical results at 5 years with reference to sex of patient, presence or absence of valvular calcification, postoperative regurgitation right ventricular hypertrophy (ECG), and quality of operation *White* = Good to excellent *shaded* = poor to fair, *black* = dead

70 per cent of the 76 patients without calcification were so considered. We do not mean to imply that calcification per se is the significant factor, but calcification associated with marked deformity and rigidity of the leaflets. and usually shortening of the subvalvular structures. It was surprising to find that the presence of regurgitation at the conclusion of operation had little effect on the outcome. In one or two instances this was true in spite of a considerable degree of postoperative regurgitation, but in the majority the insufficiency, though significant, was mild. Similarly the presence or

absence of right ventricular hypertrophy or right axis deviation in the preoperative electrocardiogram seemed to have relatively little determinant effect on the 5-year result.

Of greatest significance has been the operator's evaluation of the quality of operation; that is, the anatomic and functional result in terms of adequate size of orifice and mobility of leaflets, in addition to calcification and regurgitation. To some extent this evaluation is standardized, since the senior author participated in all operations of the entire series, but it must be acknowledged that what is accomplished by the operator in a closed mitral valvulotomy is a subjective evaluation on his part, corroborated at best by one or two assistants. When that evaluation was unequivocally excellent (42 cases), 78 per cent of the 5-year results were good to excellent. When there was some equivocation, but the quality of operation was considered good (43 cases), 49 per cent of the 5-year results were good to excellent. About the same end-results were achieved in the 13 patients in whom the operative result was considered "fair." It is in the latter two groups of cases that substantial improvement should be possible if mechanical dilatation is used to supplement digital maneuvers. The same may well be true for open operation if one assumes that removal of calcium and restoration of flexibility to the leaflets will have a lasting effect.

The problem of reoperation in patients who have undergone mitral valvulotomy is an important one. Of this series of 100 patients, 10 came to reoperation during the 5-year period of follow-up, or at some time thereafter. Rather than confine ourselves to these 10, we have thought that a more useful purpose would be served by reporting briefly our *entire* experience with reoperation for mitral stenosis. There have been 26 such operations carried out at the Massachusetts General Hospital. Eight of these operations were closed, 18 were open, using conventional methods of cardiopulmonary bypass and arrest.

The experience with closed reoperations may be briefly summarized as follows. Of a total of 8, 3 patients died of operation, 1 died 2 years postoperatively of congestive failure, 2 came to reoperation (open) at 14 and 16 months, respectively, and 2 are still doing well, 2 and 5 years after reoperation. Certainly this experience with closed reoperation was far from encouraging.

In the past 2 years we have carried out 18 open operations for recurrent mitral stenosis. The majority of these were in patients who had their initial operation at our own hospital. The average interval between initial and repeat operation was 3 years and 9 months. Six patients failed to survive. Five of these showed extreme degrees of pulmonary hypertension (the pulmonary arterial pressure equalled or exceeded the systemic) and extremely low cardiac output (Table I). Postoperatively all 5 were unable to maintain an adequate systemic pressure in spite of high peripheral venous pressure. This we have interpreted as a combination of right-sided failure and obliterative pulmonary vascular disease, making it impossible to maintain an adequate cardiac output against a high pulmonary vascular resistance. All 5 succumbed within 24 hours of operation and at autopsy were found to have had excellent operative correction of their mitral stenosis.

TABLE I

PATIENT	AGE	SEX	INTERVAL BETWEEN OPERATIONS		CALCIFICATION AT SECOND OPERATION	CALCIFICATION AT FIRST OPERATION	GOOD TO EXCELLENT SPLIT FIRST OPERATION	CATHETER FINDINGS					LIVING OR DEAD
			YR.	MO.				PAP	PAm	PC	CI	PAR	
Mu	42	F	5		+	+	+	80/35	45	25	2.4	11	L
Bu	30	F	8	8	+	Not known	Not known	80/47	63	20	0.9	48	L
Bl	39	F	2	5	+	0	0	70/34	43	32	2.2	5	L
Ga	50	F	3		+	+	0	80/40	54	38	4.4	4	L
De G	24	F	5		0	0	0	Study incomplete					L
Fi	35	F	4	10	0	0	+	90/50	65	28	2.0	17	L
No	49	M	2	11	+	+	+	65/32	43	24	2.0	10	L
Ga	28	F	1	6	0	0	+	84/38	61	31	2.8	11	L
Sw	33	M	2	11	+	+	+	—	40	15	2.0	13	L
Hy	35	F	4	2	0	Not known	Not known	40/18	25	17	2.0	4	L
St	41	M	5	1	+	+	0	No study available					L
He	43	F	7	11	0	0	0	120/50	70	27	1.5	29	L
Ha	34	F	1	4	+	+	0	110/50	65	27	2.0	19	D
Ro	19	F	5	8	0	0	0	115/58	80	25	1.7	32	D
Gr	27	F	3	9	0	0	+	Autopsy showed severe pulmonary vascular disease					D
Ho	42	F	1	7	Not known	+	Not known	120/48	62	—	—	—	D
Tu	31	F	2	5	+	0	0	59/28	39	20	2.2	9	D
Si	46	F	3	10	+	+	+	140/63	98	25	1.5	49	D

PAP = Pulmonary artery pressure (mm. Hg). PAm = Pulmonary artery, mean pressure (mm. Hg). PC = Pulmonary capillary pressure or left atrial pressure (mm. Hg). CI = Cardiac index (L/min./M.^{2}). PAR = Pulmonary arteriolar resistance—normal < 3.

Twelve patients have survived open reoperation and are presently doing well. Since the majority of these have been operated upon within the year no long-term follow-up is possible.

Of the entire series of 18 patients, calcification of the valve was pronounced in 10. Seven of these had had significant calcification of the valve at the time of their initial operation, which had been considered satisfactory in only 8 of the 18.

Returning to the original series (Table II), we find that 25 of the 100 patients had had peripheral emboli prior to operation. Twenty-one of the 25 showed atrial fibrillation at the time of operation. Of these 25, 6 had major emboli at the time of operation, 4 to the bifurcation of the aorta (all successfully removed) and 2 major cerebral emboli. Three patients of this group of 25 had late emboli; 1 at 3½ years, 1 at 20 months, and 1 had multiple visceral emboli to resume a pattern of peripheral embolization that she had exibited prior to operation. Three patients who had had no emboli prior to operation had operative emboli, 2 cerebral, 1 iliac. In addition, 2 patients without prior history of embolus had major cerebral emboli late; i.e., 4 months and 18 months after operation. That peripheral embolization is a major consideration in operative risk is indicated by the fact that of the 7 operative deaths which occurred during the period of this study, 4 were attributable to this cause.

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TABLE II. EXPERIENCE WITH PERIPHERAL EMBOLI IN 100 CONSECUTIVE PATIENTS SURVIVING MITRAL VALVULOTOMY EVALUATED AT 5 YEARS

25 patients had peripheral emboli prior to operation
  6 had emboli at time of operation
    4 saddle emboli removed successfully
    2 major cerebral emboli
      1 fair recovery; 1 poor recovery
  3 patients had late emboli postoperatively

SUMMARY AND CONCLUSIONS

The clinical result 5 years after operation has been evaluated in 100 consecutive patients surviving mitral valvulotomy. The result is considered unequivocally satisfactory, that is, good to excellent in 61; fair to poor in 20. This 5-year survival rate of 81 per cent represents a highly significant improvement over a comparable, though smaller, group of medically treated cases.

The long-term benefits of operation are most striking in patients moderately to moderately severely incapacitated by their disease, but there is a very rewarding salvage of patients severely incapacitated. The majority of poor results of operation become evident within the first year, but there is a steady attrition thereafter of recurrence of disability of about 5 per cent per year.

Three factors at the time of operation appear to have special prognostic significance: (1) the sex of the patient, the percentage of satisfactory results in women being greatly superior to that in men; (2) the presence of calcification and rigid deformity of the valves, indicating, in general, a poor prognosis; (3) the anatomic result of operation.

A review of the data suggests that the use of a mechanical dilator should improve the number of good results by increasing the number of anatomically excellent results, particularly in tough, fibrous valves. It is also a reasonable hypothesis that removal of calcium encrustations from a valve during the course of open operation may produce a greater number of satisfactory long-term results with greater initial safety than is possible at closed operation. Until the fate of decalcified valves is known, or the deposition of calcium can be controlled, this must remain supposition.

Of the present series, 10 patients have come to reoperation. The author's entire experience with 26 reoperations for mitral stenosis, 8 closed and 18 open, is briefly reviewed.

REFERENCES

1. Logan, A., and Turner, R.: Surgical Treatment of Mitral Stenosis With Particular Reference to the Transventricular Approach With a Mechanical Dilator, Lancet 1: 874, 1959.
2. Rowe, J. C., Bland, E. F., Sprague, H. B., and White, P. D.: The Course of Mitral Stenosis Without Surgery: Ten and Twenty-Year Perspectives, Ann. Int. Med. 52: 741, 1960.

(For Discussion, see page 799.)

THE TREATMENT OF ACQUIRED AORTIC STENOSIS BY VALVULOPLASTY

Donald G. Mulder, M.D. (by invitation), Albert A. Kattus, M.D. (by invitation), and William P. Longmire, Jr., M.D., Los Angeles, Calif.

The patient with acquired aortic stenosis remains a challenging surgical problem. Attempts to relieve the valvular obstruction by the currently recommended techniques have not been consistently successful. Our experience with the "blind" transventricular commissurotomy and the "open" direct vision commissurotomy has been disappointing Unless these calcified, rigid valves can be mobilized, little functional benefit may be anticipated. Removal of the calcific deposits, originally suggested by Bailey,[1] will accomplish this objective. A technique has been developed for débriding the aortic cusps of the crucial, obstructing encrustations and for reconstructing the valve, when necessary, which we have referred to as aortic valvuloplasty.[2]

SELECTION OF CASES

Patients were selected for operation on the basis of clinical evaluation and the hemodynamic data obtained by left heart catheterization. Operation was not considered indicated unless the patient presented with symptoms of syncope, left ventricular failure, or angina. Progressive left ventricular enlargement on roentgenograms and electrocardiographic evidence of left ventricular hypertrophy were strong indications for operation. Calcification of the aortic valve and dilatation of the ascending aorta were confirmatory findings but were not considered essential.

Preoperative evaluation of potential surgical candidates by measurement of the pressure gradient across the aortic valve was considered to be essential to establish the diagnosis. The occasional patient with a classical "aortic stenosis murmur" caused by a diseased but nonobstructed aortic valve, who has angina due to coronary artery disease, will thus be spared a futile thoracotomy Simultaneous cardiac output determinations have not been performed routinely. We still consider a gradient across the aortic valve of 50 mm Hg or more as indicative of significant valvular obstruction. Under certain circumstances, such as a severely ill patient with a low cardiac output, operation has been advised despite a lower gradient. The presence of heavy aortic valvular calcification, associated multivalvular disease or acute cardiac decompensation, does not contraindicate surgical intervention, although the operative risk in these patients is greater

However, active rheumatic fever or subacute bacterial endocarditis is definite contraindication to surgery

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TABLE I. CLINICAL AND HEMODYNAMIC EVALUA

	CLINICAL FINDINGS							X-RAY		
PATIENT	AGE AND SEX	HISTORY OF RHEUMATIC FEVER	HISTORY OF CHILDHOOD MURMUR	CHEST PAIN	SYNCOPE	DYSPNEA	HEART FAILURE	AORTIC VALVE CALCIFICATION	LEFT VENTRICULAR ENLARGEMENT	DIAG
E. B.	43 M	0	0	0	++	++	0	++	0	A. S.
R. C.	49 M	+	0	++	++	+++	++	+++	++	A. S. A. I.
J. F.	42 M	+	0	0	+	++	++	++	++	A. S. M. S.
R. F.	45 M	0	+	++	0	++	+	++	+	A. S.
B. G.	30 M	0	+	+	0	+	0	+++	+	A. S.
L. W.	48 M	0	0	0	+	++	+	+++	++	A. S.
N. W.	39 M	0	0	++	0	++	0	+++	++	A. S.
D. Y.	17 M	?	0	+	0	+	0	0	0	A. S.
A. G.	35 M	0	+	0	?	++	0	+++	+++	A. S. A. I.
C. B.	46 M	+	+	+	0	++	+++	+++	+++	A. S. A. I.
H. M.	50 M	0	+	0	+	+	0	++	+++	A. S. A. I.
C. N.	23 M	?	0	+	0	++	0	0	++	A. S.
C. O.	55 M	0	0	++	++	++	0	++	++	A. S.
G. P.	48 M	+	+	++	+	+++	+	++	++	A. S.
W. V. N.	44 M	0	0	++	+	+++	+	+++	++	A. S.
B. J.	37 M	+	0	++	0	+++	0	+++	++	A. S.
M. W.	42 F	+	0	+	0	++	0	+++	++	A. S. A. I.
G. C.	46 M	0	0	++	++	+++	+	++	++	A. S.

Legend: A.S. = Aortic stenosis. M.S. = Mitral stenosis. A.I. = Aortic insufficiency.

PREOPERATIVE EVALUATION OF PATIENTS

Eighteen patients (Table I) represent our total experience to date in the treatment of acquired aortic stenosis by the operative procedure to be described. Five patients had significant to severe associated aortic insufficiency. There were 17 males and 1 female. The average age of the patients was 41.1 years. A murmur had been noted in childhood in 6 patients. A history of rheumatic fever was obtained in 6 patients, with a questionable history in 2 additional patients. These 2 patients, the youngest in the group, were the only ones who did not have gross, calcific valvular deposits. The disease did not appear to be of congenital origin because the valves were markedly thickened, rolled, and relatively rigid with fusion of the commissures. Furthermore, no murmur had been detected in childhood in these 2 cases. All patients gave a history of syncope, left ventricular failure, or chest oup of Patients With Acquired Aortic Stenosis

PRESSURE MEASUREMENTS ACROSS AORTIC VALVE						RESULTS	
PREOPERATIVE		POSTOPERATIVE		GRADIENT (MM. Hg)			DURATION OF FOLLOW-UP (MONTHS)
EFT TRICLE	ARTERIAL	LEFT VENTRICLE	ARTERIAL	PRE-OPERATIVE	POST-OPERATIVE		
4/0	100/56	112/4	112/56	74	0	Excellent	17
0/34	96/49	104/8	100/57	54	4	Excellent	16
0/30	120/60	103/8	100/62	60	3	Excellent	15
8/0	102/70	120/4	110/75	36	10	Excellent	12
0/10	110/70	148/4	140/88	90	8	Excellent	10
0/25	150/60	148/6	148/70	100	0	Excellent	9
5/10	110/60	148/8	120/72	115	28	Excellent	9
0/0	130/70	120/0	120/80	50	0	Excellent	12
0/10	108/50	92/0	92/64	132	0	Excellent initially; died 7 months postoperative with acute bacterial endocarditis	7
4/12	110/48	130/4	130/66	84	0	Excellent	8
6/30	85/38	130/4	110/52	181	20	Excellent	8
0/0	115/70	120/0	112/60	95	8	Excellent	6
0/0	110/60	—	—	(90)	—	Died at operation; irreversible fibrillation; calcium embolus to left coronary	–
30/0	130/77	90/4	90/70	50	0	Excellent	4
53/0	104/64	100/0	100/68	149	0	Died 3 days postoperative from severe central nervous system injury	–
86/0	116/60	110/4	104/65	70	6	Died suddenly 1 hour postop.; acute occlusion left coronary by embolic calcium fragment	–
20/10	120/52	140/10	140/85	100	0	Excellent	2
10/0	106/64	100/0	100/52	104	0	Died 2 weeks postoperative from severe central nervous system injury	–
			Average	90 mm. Hg	5 mm. Hg		

pain. Two patients had a questionable history of myocardial infarction. Roentgenographic examination revealed calcification of the aortic valve in 16 patients, and left ventricular enlargement was demonstrated in sixteen instances. Electrocardiographic evidence of left ventricular hypertrophy was present in every case.

Simultaneous pressure measurements in the left ventricle and femoral artery were made in all patients preoperatively (Fig. 1). The systolic gradient across the aortic valve ranged from 36 to 181 mm. Hg with an average of 90 mm. Hg. Simultaneous cardiac output studies were occasionally but not routinely performed.

OPERATIVE TECHNIQUE

The patient is placed supine and anesthetized with Pentothal sodium, nitrous oxide, and oxygen. The electroencephalogram and electrocardiogram are continuously monitored. The systemic arterial pressure is recorded through a right radial artery cannula, and the superior vena cava pressure via a cardiac catheter passed up the right antecubital vein. Vasopressors are administered, if necessary, to maintain a satisfactory arterial pressure. Ventricular fibrillation is prone to occur in these patients if hypotension and lowered cardiac output occurs and is not promptly corrected.

A median sternotomy incision is preferred, which gives good exposure to the base of the heart and great vessels. The thymus is dissected off the pericardium and divided between its lobes up to the innominate vein. The pericardium is opened anteriorly to the right phrenic nerve, and the incision curved over the base of the great vessels toward the apex of the heart. Two purse-string sutures of 3-0 arterial silk are placed in the right auricular appendage. In the more critically ill patients, the right common femoral artery is exposed at this point through a longitudinal incision in the groin. After heparinization (1.7 mg. per kilogram), the patient is connected to the extracorporeal circuit (modified Kay-Cross disc oxygenator) by insertion of the femoral arterial cannula. The superior and inferior venae cavae and the aorta can now be safely dissected free and encircled with tapes, since cardiopulmonary bypass may be initiated without delay should the patient's condition deteriorate during

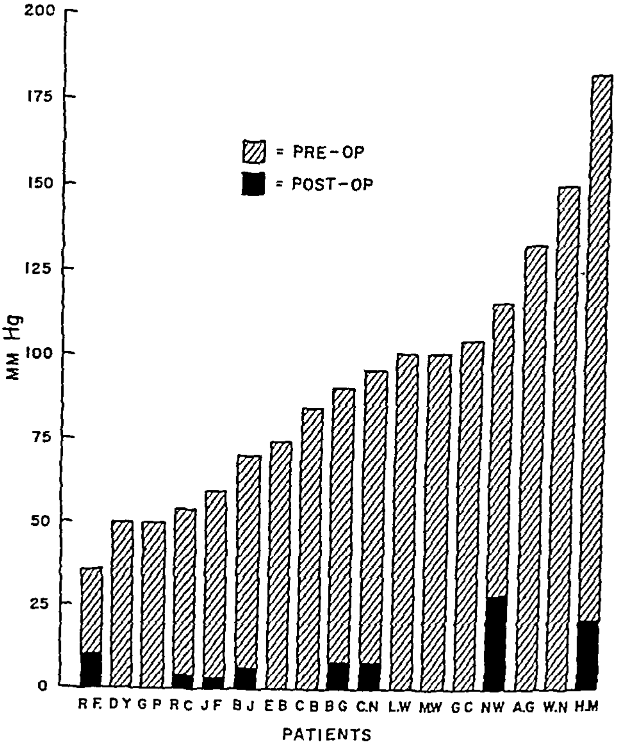

Fig. 1.—Bar graph which depicts the preoperative and postoperative systolic gradients across the aortic valve. One patient died at operation and no postoperative measurements were made.

manipulation of the heart and great vessels. After a short stabilization run on full bypass, the ascending aorta is cross-clamped. The proximal ascending aorta is promptly opened through a longitudinal incision which is curved posteriorly (Fig. 2, *A*). The right coronary artery must be identified to spare it from injury. This hockey-stick incision gives satisfactory exposure (Fig. 2, *C*) and lessens the likehood of tearing the aortic incision by excessive retraction. The right and left coronary ostia are quickly identified and specially constructed perfusion cannulas are introduced (Fig. 2, *B*). In the initial 11 cases the heart was allowed to go into ischemic arrest. Currently, selective hypothermic coronary perfusion is used, although no instance of myocardial damage related to the former method was encountered. Approximately 1,200 to 1,500 c.c. of oxygenated, heparinized, hypothermic (15° C.) blood is perfused during a 5- to 7-minute period using an auxiliary De Bakey pump. Cooling is accomplished by passing the blood, which is diverted from the oxygenator, through a coiled polyethylene tubing submerged in ice-water. The blood is returned to the pump circuit by a right atrial cannula, or aspirated as it returns to the left ventricle. During the local cardiac cooling, the valvular deformity is carefully evaluated. The coronary perfusion cannulas are removed and attention is directed to repair of the valve.*

The critical obstructing and immobilizing encrustations are then removed by the following technique: An incision is made through the thickened endothelium along the base or annulus side of the calcific deposit (Fig. 3). An endarterectomy Freer elevator is used to establish the proper cleavage plane between the calcific mass and the underlying valve tissue. The débridement is made easier and more effective by starting at the base of the plaque deep in the cusp sinus. Although more difficult to visualize initially, it accomplishes two things: (1) the freed valve cusp does not tend to fold and lose its stability as the remainder of the encrustation is removed, and (2) no valve tissue is sacrificed by an incision into the leading edge of the calcareous mass, which may be partially covered by the rolled up cusp margin.

Care must be taken to prevent perforation of the diseased valve (Fig. 4, *A*, *B*, *C*). Spotty areas of through-and-through degeneration of the valve may not be apparent when viewed from the aortic side, but can be recognized by a dimpled area on the ventricular aspect of the valve; this must be débrided cautiously. Calcifications occur most commonly on the aortic side of the valve but may occur on the ventricular side as well. Occasionally, the coronary ostia are encroached upon by plaques; these should also be removed. Fibrous fusion at the commissures is incised by knife, either completely to the aortic wall or nearly so, depending upon the adequacy of the valve tissue. A tricuspid or biscuspid valve is fashioned as indicated by the valvular deformity in the individual case. Removal of the calcific crags often results in "unrolling" of the cusps so that the frequently associated aortic insufficiency may also be corrected. In other instances, after mobilizing the valve, it will still be necessary to form a bicuspid valve to achieve competency (Fig. 5, *A*, *B*).

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*Continuous perfusion of only the left coronary artery with normothermic blood has been used in recent cases and, at present, is the technique we prefer.

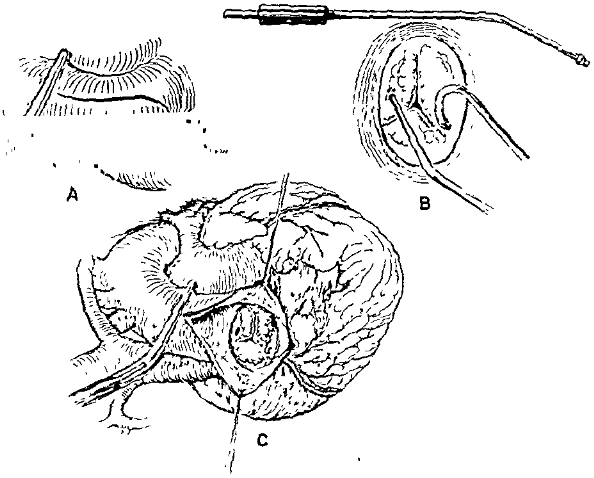

Fig. 2.—*A*, A longitudinal hockey-stick aortic incision is made.

B, Stainless steel coronary perfusion cannulas are inserted into the right and left coronary ostia, and the heart is perfused with oxygenated, hypothermic blood.

C, Good exposure is obtained with this incision which lessens the liklihood of tearing the edges of the aortic incision.

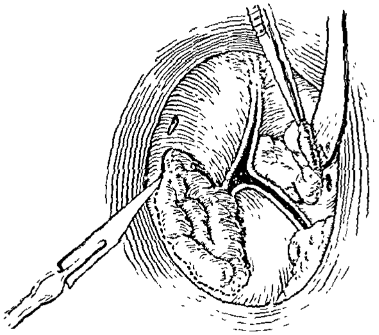

Fig. 3.—An incision is made at the base of the plaque. An endarterectomy Freer elevator is used to develop the proper plane between the calcareous mass and the underlying valve tissue.

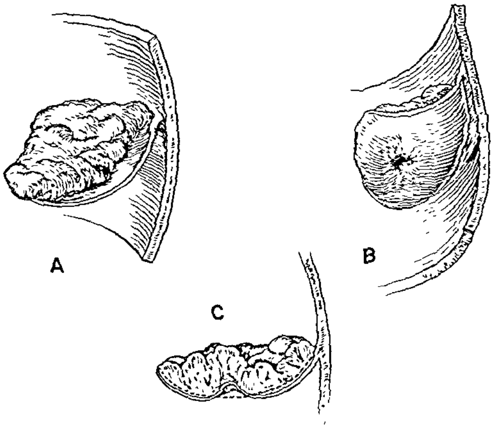

Fig. 4.—*A-C*. Three views of a diseased aortic valve cusp. No indication from aortic aspect *(A)* that dimpled area of through-and-through degenerative change is present which is apparent from ventricular aspect *(B)*. Cusp perforation *(C)* will result if radical removal of entire calcareous deposit is attempted.

Partial replacement or reinforcement by the insertion of a prosthetic cusp is occasionally indicated (Fig. 5, *C, D*). Decreasing the circumference of the aortic annulus by "taking a tuck" in the wall at one commissure has also been an effective method of correcting the associated aortic insufficiency (Fig. 6).

After the valvuloplasty has been completed, the left ventricle and root of the aorta are flushed with saline, the suture line is partially closed, and the remaining aortotomy is excluded with a Satinsky clamp. The aortic cross-clamp is then released and the patient is placed in parallel with the pump circuit by releasing the occluding vena caval snares. This prevents distention of the nonbeating heart by decompressing the coronary sinus blood into the caval catheters. The left ventricle and left atrium are carefully observed for distention which would indicate significant aortic insufficiency. If this occurs, the patient is promptly returned to full bypass and the repair revised, for

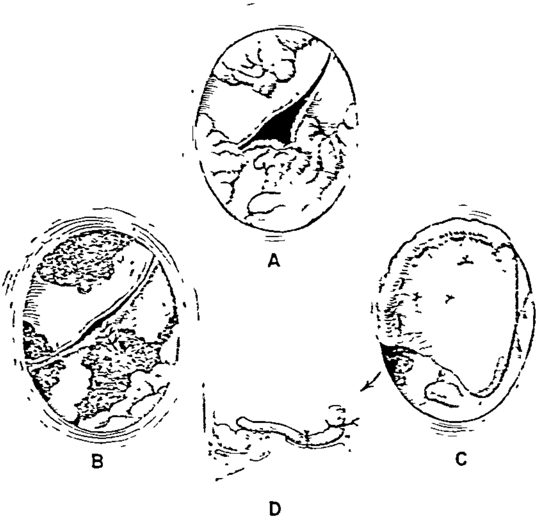

Fig. 5.—*A*, Typical deformed aortic valve with calcified encrustations which cause valvular stenosis and insufficiency.

B, After mobilizing the valve cusp, bicuspidization may achieve valvular competence as well as relieve obstruction.

C and *D*, When remaining valve tissue is inadequate despite débridement, prosthetic cusp is inserted.

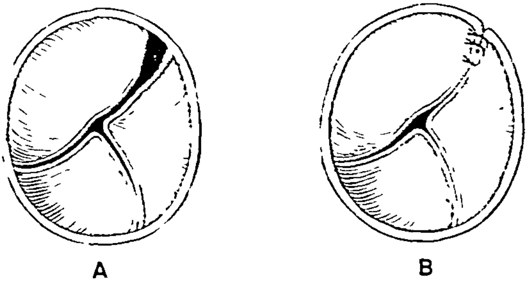

Fig. 6.—*A*, Aortic insufficiency may be due to defective valve tissue in one commissural region and/or annular dilatation.

B, "Annular tuck" technique will restore valvular competency.

it is virtually impossible to resuscitate the heart if significant aortic insufficiency is present. Following restoration of coronary blood flow, the heart action may return with a normal rhythm, but usually ventricular fibrillation is present which is reverted by electric shock.

As soon as the heartbeat is adequate, the extracorporeal circulation is discontinued, the aortotomy closure is completed, and all cannulas are removed Protamine (2.0 mg. per kilogram) is given and the atrial and arterial incisions are repaired. The right pleural space is opened widely to accommodate any postoperative bleeding, and two chest catheters are inserted. The pericardium is left open. Prior to closure of the chest, repeat measurements of the left ventricular and systemic arterial pressures are performed.

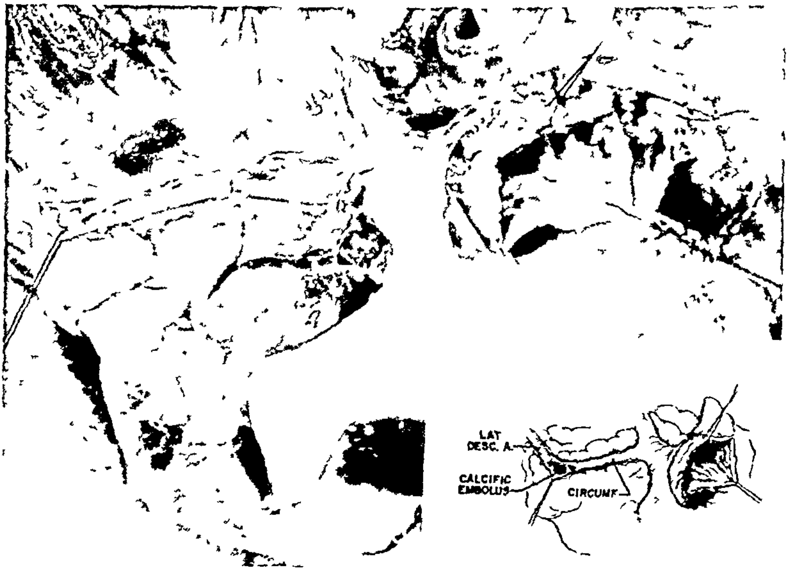

Fig 7—Finding at autopsy in patient (B J) who died suddenly 1 hour postoperatively An embolic calcific fragment from the aortic valve completely occluded the left lateral descending coronary artery

RESULTS OF OPERATION

There were four operative deaths among these 18 patients, a mortality rate of 22 per cent. One patient (C. O.) failed to survive the operative procedure. Removal of several large deposits of calcium had resulted in quite adequate aortic cusp mobility. As the operation was being completed, however, the heart action suddenly became very poor and ventricular fibrillation ensued which was irreversible At autopsy, a fragment of calcium which had embolized from the valve was found to be completely occluding the left circumflex coronary artery. A similar cause of death was present in 1 other patient (B. J.), who died 1 hour postoperatively. Again the valvular reconstruction had been satisfactory. The patient was awake and maintaining a normal blood pressure when he suddenly developed irreversible ventricular fibrillation. In this instance the calcium embolus totally occluded the left lateral descending coronary artery (Fig. 7).

Two patients died from severe, progressive central nervous system damage, 3 days (W. V. N.) and 2 weeks (G. C.), postoperatively. The latter patient also had a massive upper gastrointestinal tract hemorrhage 6 days after operation and went into profound shock. Despite fresh blood replacement, the bleeding persisted and the patient underwent laparotomy. Suture ligation of a bleeding duodenal ulcer, pyloroplasty, and vagotomy were performed. Although he tolerated this episode surprisingly well, his condition steadily deteriorated neurologically, and he died 7 days following the second operation. At autopsy, no calcium emboli to the cerebral circulation could be demonstrated. However, large intravascular fat globules (Fig. 8) were noted in histologic sections of the brain. Whether these are related to the brain injury or not is speculative. An additional possibility is the ever-present hazard, especially in the treatment of lesions on the left side of the heart, of air embolism.

There was one late death (A. G.) which occurred 7 months after operation. This patient developed a bacterial endocarditis in the early postoperative period and was treated intensively for 6 weeks. At this time he was afebrile and blood cultures were negative. He returned to full activity and seemed to be doing very well until 1 week prior to his death when he developed a fulminating, recurrent bacterial endocarditis (Fig. 9).

Two patients (C. N. and G. P.) bled postoperatively from their aortotomy and re-exploration was necessary. Their subsequent convalescence was uncomplicated.

A bicuspid valve was initially present or created by suture obliteration of one commissure in 12 patients. A tricuspid valve was present or created by developing the obliterated commissure in 6 patients. Partial cusp replacement by a piece of compressed Ivalon was used in one instance (H. M.) to correct a moderately severe associated aortic insufficiency.

The 13 surviving patients have been followed from 2 to 17 months (average 10 months). The improvement in the physiologic classification of the cardiac status of these patients as determined by the criteria of the New York Heart Association is shown in Table II. Four patients were improved from Class IV to Class I, 2 patients were improved from Class IV to Class II, 5 patients were improved from Class III to Class I, and 2 patients were improved from Class II to Class I. There have been no syncopal episodes after operation, although 1 patient (H. M.), who had a history of a previous stroke, had a second stroke 2 months postoperatively. A transient hemiplegia was present for several days which cleared completely.

TABLE II. PHYSIOLOGIC IMPROVEMENT IN CARDIAC STATUS FOLLOWING VALVULOPLASTY

PREOPERATIVE	POSTOPERATIVE	NUMBER OF PATIENTS
Class IV	Class I	4
Class IV	Class II	2
Class III	Class I	5
Class II	Class I	2

A systolic murmur of decreased intensity remains in every case. Two patients have a residual diastolic murmur of aortic insufficiency.

At operation, prior to closure of the chest, repeat pressure measurements were obtained from the left ventricle and a systemic artery (see Table I). The postoperative systolic gradient across the aortic valve ranged from 0 to 28 mm. Hg with an average of 5 mm. Hg. In those patients in whom the gradient was essentially abolished, the contour of the arterial pulse wave became relatively normal (Fig. 10). The classical anacrotic notch and slow "time to peak" of the arterial pulse tracing reverted postoperatively to a more normal contour.

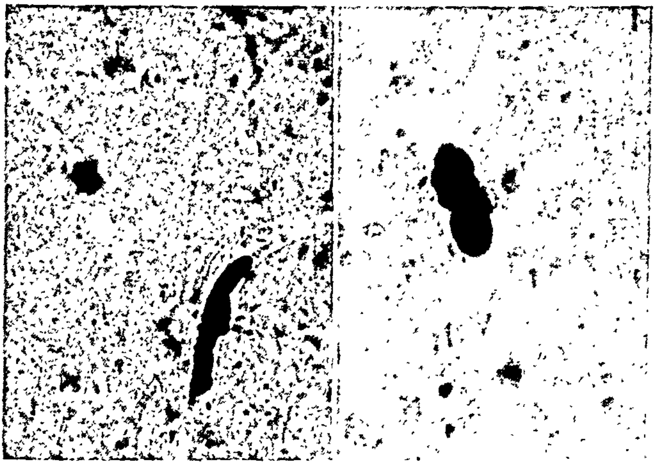

Fig. 8.—Histologic section of brain in patient (W. V. N.) who died 2 weeks postoperative from severe, progressive central nervous system damage. Large intravascular globules of fat are seen which were present throughout the brain.

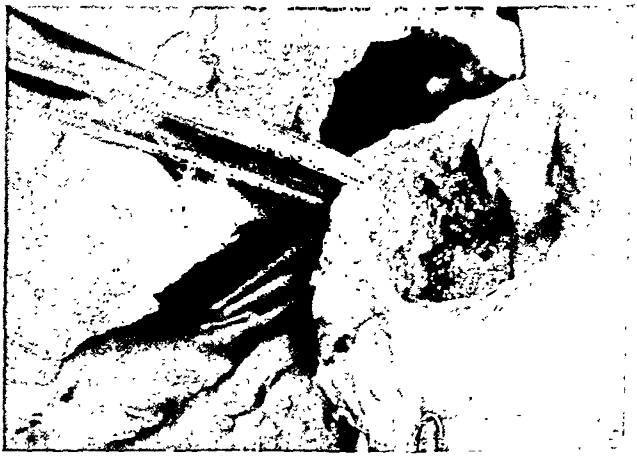

Fig. 9.—Gross vegetations can be seen on aortic valve of patient (A. G.) who died 7 months after operation from fulminating, recurrent bacterial endocarditis.

DISCUSSION

There are those who continue to advocate the use of closed techniques in the surgical treatment of acquired aortic stenosis.[3, 4] A low operative mortality, gratifying clinical improvement, and generally favorable hemodynamic changes have been reported.

Division of the commissures under direct vision using hypothermia as performed by Swan[5] and Lewis,[6] or using extracorporeal circulation as initiated by Lillehei,[7] have been accepted techniques.

The disadvantage of not being able to see and evaluate precisely what is being done to the valve during closed procedures would seem to be a significant one. Furthermore, it is not possible to correct the frequently associated aortic insufficiency; in fact, it may be made worse with this type of operation. Separation of the commissures under direct vision can be performed within the time limits of hypothermia. The addition of cardiopulmonary bypass would seem unnecessary if the objective of the procedure is only to cut or break open the commissures.

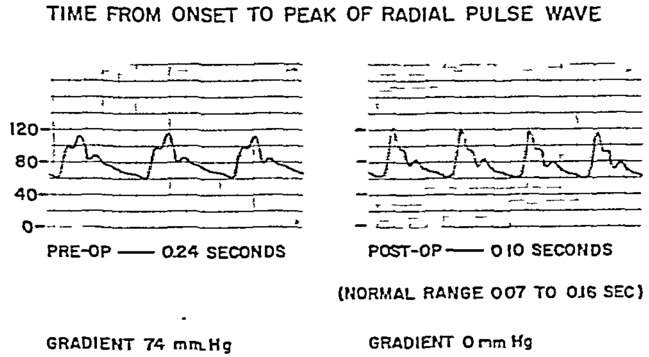

Fig. 10.—Changes in arterial pulse wave contour following valvuloplasty. Note the typical delayed "rise time" and anacrotic notch preoperatively compared to normal slope and contour of wave after operation.

We would agree with the concept of Bailey,[5] that only by removing the immobilizing calcific masses on the valve will cusp mobility be restored. In addition, added valve cusp length, sufficient to correct an associated valvular incompetence, may be gained as the plaques are removed and the underlying valve tissue is "unrolled." Unrelieved or surgically created aortic insufficiency is very poorly tolerated by the heart and may prevent its resuscitation. We have had no difficulty in re-establishing a normal beat in 11 patients who have had as long as 40 minutes of normothermic, ischemic arrest, providing a definite hemodynamic improvement was achieved. In no instance were there any late sequelae suggesting myocardial injury. In other patients (with pure aortic insufficiency) in whom the valvular incompetence was not satisfactorily corrected, restoration of heart action has been impossible following much shorter periods of arrest. Selective cardiac cooling has recently been adopted because of the reported myocardial protection it affords during prolonged cardiac arrest.*

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*No longer used.

In this group of patients, it was always possible to remove much of the calcium from the cusp surface. The extent to which this can be accomplished will vary in each case, depending upon the severity of the degenerative valvular changes. A most gratifying restoration of function will be achieved in many instances where removal of two or three struts of valvular calcification restores the hinge action to the cusp. Occasionally, the valve will be almost replaced by a conglomerate mass of rock-like crags. Cautious, partial débridement of these amorphous encrustations often fails to restore sufficient cusp mobility to abolish completely the obstruction. Most commonly, the disease process falls between these two extremes, and the quality of the reconstructive procedure certainly is related in some degree to the severity of the valvular deformity. Regardless of certain limitations, it has been made possible, without exception, by painstaking removal of these plaques alone or in combination with additional valvular reconstruction (bicuspidization, annular tuck, prosthetic cusps), to improve distinctly aortic valve function.

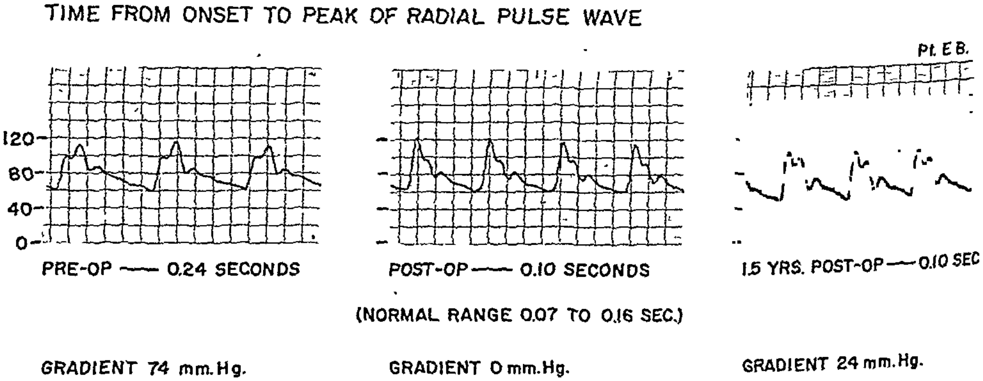

Fig. 11.—Repeat left heart catheterization in patient (E. B.), 1½ years postoperatively. Contour of arterial pulse wave remains normal. A gradient across the valve of 24 mm. Hg was recorded.

Total replacement would appear to be the ultimate ideal in the treatment of those patients with hopelessly destroyed aortic valves. Currently, such a clinically proved prosthesis is not available, but almost certainly will be in the near future. Even so, it is questionable whether the insertion of a foreign body at such a critical point in the cardiovascular system would be indicated in every case of aortic stenosis. For, if the patient's own valve can be restored to adequate function, this may be preferable to the insertion of a prosthesis.

The long-term results of this technique are still not known. There is no assurance that continued deposition of calcium and re-stenosis will not occur. Recatheterization of our first patient (E. B.), 1½ years postoperatively has been encouraging in this regard (Fig. 11). Preoperatively, he had a gradient across the aortic valve of 74 mm. Hg with a "time to peak" of the systemic arterial pulse wave of 0.24 second with the anacrotic notch typical of patients with aortic stenosis. Immediately postoperative, the gradient was completely abolished and the arterial pulse wave contour was normal with a "time to peak" of 0.10 second. One and one-half years later, he still has a normal pulse contour indicating no detectable delay in left ventricular emptying, although a gradient across his valve of 24 mm. Hg was demonstrated.

The future course and hemodynamic evaluation of these patients will be essential in order to assess the value of this procedure in the treatment of patients with acquired aortic stenosis.

SUMMARY

Eighteen patients with acquired aortic stenosis have been treated by aortic valvuloplasty during extracorporeal circulation.

The obstructing calcareous deposits were dissected from the valve tissue which resulted in relief of the obstruction and restoration of cusp mobility.

All patients presented with symptoms of syncope, left ventricular failure or angina, and demonstrated transvalvular pressure gradients averaging 90 mm. Hg.

There were four operative deaths: in two instances due to severe central nervous system injury, and in two instances to calcific emboli to the coronary arteries. One late death (7 months) was due to bacterial endocarditis.

The 13 survivors have all shown symptomatic improvement, and their average residual pressure gradient is 5 mm. Hg.

Hemodynamic measurement 1½ years postoperatively in 1 patient indicated that his operative improvement had been maintained.

REFERENCES

1. Bailey, C. P.: Discussion of Harken et al.[4]
2. Mulder, D. G., and Winfield, M. E.: Valvuloplasty for Acquired Aortic Stenosis, Ann. Surg. 151: 203, 1960.
3. Glover, R. P., and Gadboys, H. L.: Seven Years Experience With Transventricular Aortic Commissurotomy, J. THORACIC SURG. 36: 839, 1958.
4. Harken, D. E., Black, H., Taylor, W. J., Thrower, W. B., and Soroff, H. S.: The Surgical Correction of Calcific Aortic Stenosis in Adults, J. THORACIC SURG. 36: 759, 1958.
5. Swan, H., and Kortz, A. B.: Direct Vision Trans-Aortic Approach to the Aortic Valve During Hypothermia: Experimental Observations and Report of Successful Clinical Case, Ann. Surg. 144: 205, 1956.
6. Lewis, F. J., Shumway, N. E., Niazi, S. A., and Benjamin, R. B.: Aortic Valvulotomy Under Direct Vision During Hypothermia, J. THORACIC SURG. 32: 481, 1956.
7. Lillehei, C. W., Gott, V. L., DeWall, R. A., and Varco, R. L.: The Surgical Treatment of Stenotic or Regurgitant Lesions of the Mitral and Aortic Valves by Direct Vision Utilizing a Pump-Oxygenator, J. THORACIC SURG. 35: 154, 1958.
8. Bailey, C. P., and Zimmerman, J.: Advances in the Surgical Treatment of Aortic Stenosis and Incompetence in Advances in Cardiology, Basal/New York, 1959, S. Karger, vol. 2, p. 20.

(For Discussion, see page 793.)

PARTIAL AND COMPLETE PROSTHESES IN AORTIC INSUFFICIENCY

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Diseases of the aortic valve present many anatomic and clinical syndromes Aortic insufficiency with a dilated left ventricle in failure has been totally refractory to surgical intervention. Because of the clear diagnosis and grave prognosis of these patients, we are not only eager to intervene but have an obligation to undertake whatever we may regard as the most reasonable therapy. It is to this group that we address ourselves here.

Our efforts in treating aortic insufficiency have been in four categories: (a) circumclusion of the base of the aorta[12]; (b) direct plastic repair of the cusps; (c) Teflon* cusp extension; and (d) valve replacement with complete prosthesis.

CORRECTION WITHOUT PROSTHESES

Some years ago[12] we described a technique for *circumclusion* by placing a tapered suture that enlarged to a woven silk band around the dilated base of the aorta. This passed beneath the coronary ostia and, when drawn up, could reduce insufficiency by bringing cusps into better apposition. The anatomic and pathologic concepts of aortic insufficiency described in this connection have been useful.

We have not been successful with *direct plastic procedures* in patients with dilated ventricles in failure. Two patients have had this procedure. In each of these, the mobile noncoronary cusp was advanced into the central zone of insufficiency by suturing the right and left coronary cusps, respectively, to the commissure on either side of the noncoronary cusp. The commissure between the two coronary bearing cusps was then partially closed by sutures (Fig. 1).

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*C. R. Bard, Inc, Summit, N J.

This reduced or eliminated regurgitation. Leaflet flexibility remained in the noncoronary cusp. The first patient could not be resuscitated after closing the aorta. The second patient had a more compact ventricle and did survive 36 hours but died suddenly. On the pulse duplicator at autopsy both had some degree of stenosis, although not of the size generally regarded as critical. According to Laplace's law, $T = P \times R$.* Therefore, if any gradient is produced across the valve it may cause fatal elevation in intramural tension in ventricles with large radii. This seemed to explain these failures. This concept must be borne in mind when "bicuspidalization" or other plastic procedures are considered.[13-15] Since this experience, we have used existing valve tissue only where the continuity of leaflets has been interrupted by subacute bacterial endocarditis or trauma.

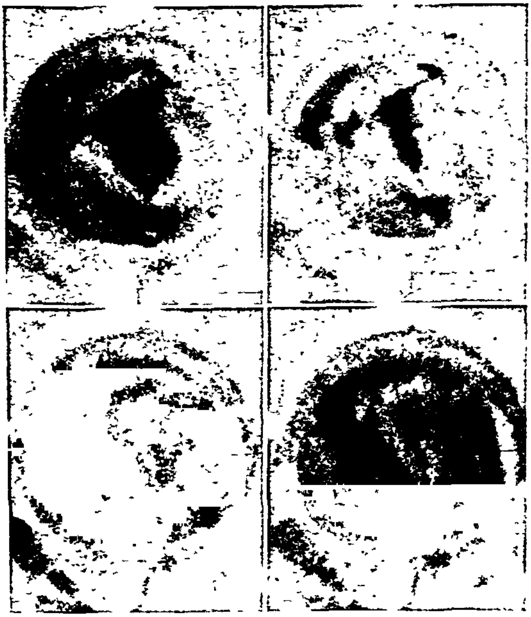

Fig. 1.—Pulsator films of aortic valve in autopsy specimen. A direct valvuloplasty was performed which corrected the aortic insufficiency but produced stenosis. The noncoronary bearing cusp is the cusp at the right.

The limitations of these plastic procedures led us to work on cusp substitution, then cusp extension, and eventually valve replacement.

Cusp substitution seemed feasible on the pulse duplicator and in the experimental animal. Teflon cloth seemed to be the most suitable material. It flexed well and could be solidly placed after excision of the neutral cusp. Others have had encouraging experience.[16, 17] However, Teflon cloth was abandoned for fear that it might become infiltrated with fibrous tissue and contract or roll into a stiff scar allowing regurgitation and stenosis. We even planted Teflon cloth in the abdominal wall of animals long enough to constitute a form of autograft. This, too, presumably has the disadvantages of late contraction and stiffening.

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*Where T = intramural tension. P = pressure. and R = radius of the chamber.

CUSP EXTENSION

Nonwettable cusps of Teflon or polyurethane were unattractive in view of our experience with embolization from clot propagated at the junction of the endocardium with Lucite balls, bottles, and spindle baffles in mitral insufficiency.[18] Furthermore such materials require long fatigue tests. For example, if the opening and closure of a valve is one cycle, a heart rate of 100 beats a minute will undergo more than 50 million cycles a year. The testing equipment that we are using now cycles from 1,000 to 2,000 times a minute.

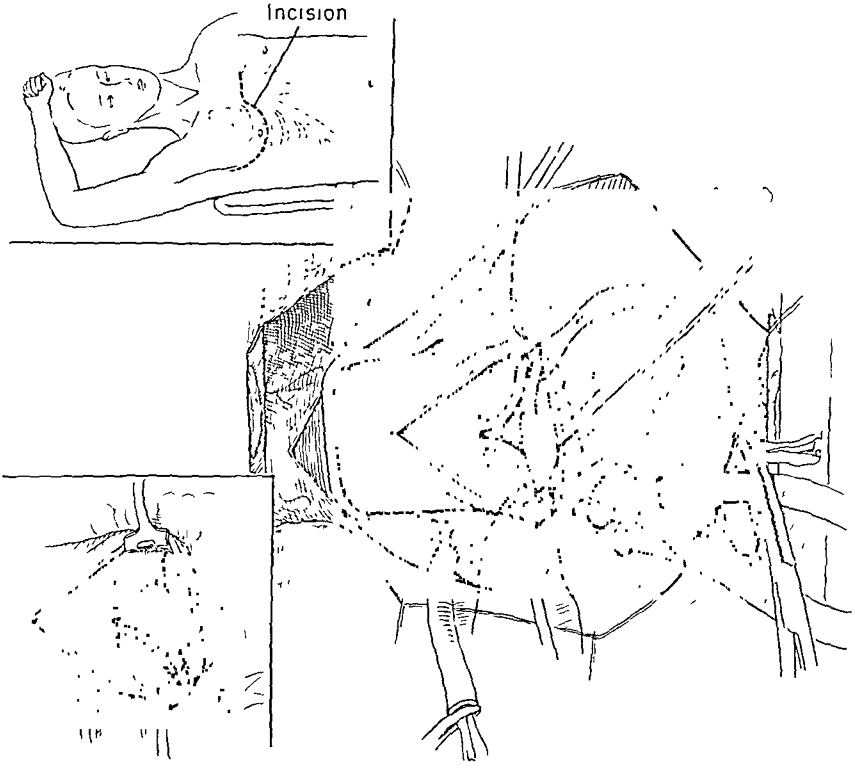

Fig. 2.—Extension of the neutral cusp. This technique was subsequently altered. A double thickness of Teflon patch was used to sandwich the edge of the leaflet so to prevent the sutures from cutting through.

Further acceleration seems impractical. Even this device has only recently been developed. Thus no flexion testing equipment has been available to give adequate information quickly.

Under these circumstances we have been eager to fatigue test material yet explore stiff cusp extension techniques that utilize the flexibility of the leaflets of the patient's heart and block reflux with a stiff woven Teflon patch extension (Fig. 2).

The noncoronary bearing or "neutral" cusp is not only the most mobile leaflet, but it has a characteristic position when the aortic valve becomes incompetent. It drops downward and backward. It may be incompetent by a loss of substance centrally, by backward displacement, or by aortic base enlargement transversely. Also, as it falls to a lower level, incompetence is produced longitudinally (Figs. 3 and 4). This cusp is also in a right posterolateral position so that it and the corresponding sinus of Valsalva are accessible to surgical approach. Prosthetic extensions to this cusp therefore fall nicely below the coronary ostia. Finally, there is often fusion of the commissures between the coronary bearing cusps that serve as an excellent base against which the valve extension can seat.

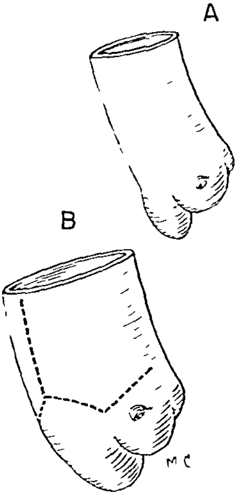

Fig. 3.—*A*, Profile of normal aorta indicating the lower position of the neutral cusp. *B*, Profile of aorta in aortic insufficiency indicating widening of the base and herniation of the neutral cusp.

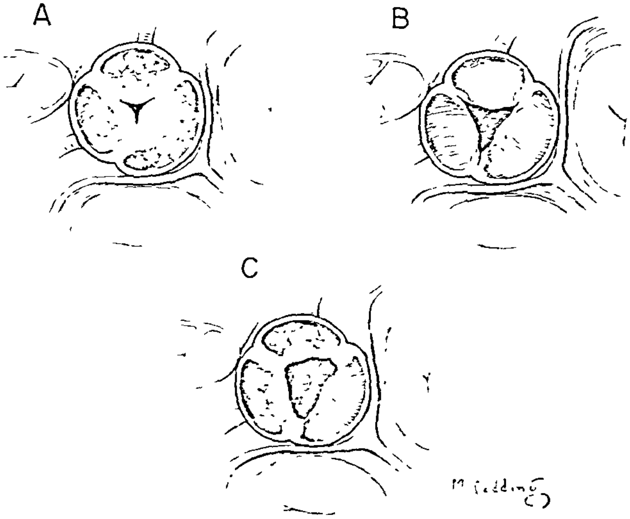

Fig. 4.—Common pathologic patterns of aortic insufficiency. *A*, Combined calcific aortic stenosis and insufficiency. *B*, Predominant aortic insufficiency, noncalcific. *C*, Predominant aortic insufficiency, calcific and noncalcific.

There have been four Teflon *cusp extension* operations. Of these 4 patients, 1 succumbed as the aorta was closed and the back pressure from the pump invaginated the extension. This was prevented in other patients by a pull-through traction suture placed at the apex of the Teflon that could be removed after closure of the aorta. Three other similar operations were performed and all patients survived. One of these patients died a year after his operation. He had done well for 10 months, then suddenly developed free aortic insufficiency and died soon thereafter in congestive failure. At autopsy the sutures were found to have cut through the cusp and released the Teflon extension. Subacute bacterial endocarditis in the interim may have contributed to the erosion and loss of the leaflet extension, but this loss was probably due to the fact that only a single layer of Teflon was sutured to the free margin of the noncoronary bearing cusp (see Fig. 2). In subsequent operations the leaflet edge was sandwiched between two thicknesses of Teflon functionally similar to the original. Both of these patients are doing quite well 8 and 12 months after operation. Both are palliated and clinically improved. Neither have had complete correction of their regurgitation.

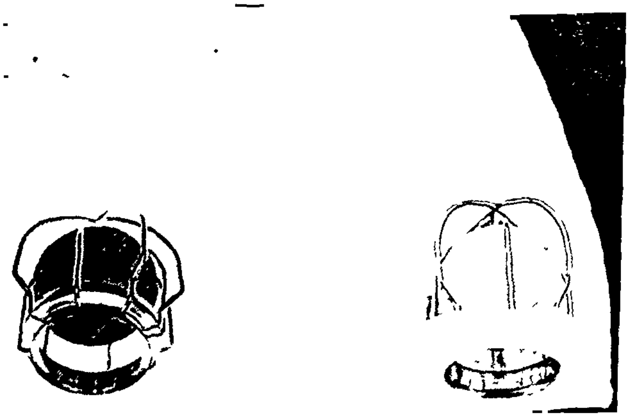

Fig. 5.—Caged-ball valve. Valve sutured in Ivalon.

THE CAGED-BALL VALVE

As no Teflon leaflet extension was curative, we turned to the construction of a complete valve. In view of difficulties with fatigue studies, we sought materials that have been tested, namely, the Lucite balls of the Hufnagel valve,[19] or preferably the more recent, quiet, silicone rubber-covered ball. These have been in place in human beings since 1955.[20]

A stainless steel caged-ball valve has been built (Fig. 5).* The orifice is 1.98 sq. cm. The inner cage must allow the ball to move far enough away from the base so that it does not obstruct flow, but if it is too long the ball can move so far away that there may be delay in return and, thus, reflux. The inner cage is of close tolerance for rapid seating.

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*Davol Company, Providence, R. I.

Studies of pulse contour indicate that the dimensions of this valve fulfill the hemodynamic requirements. With such narrow tolerance the ball extends beyond the inner cage and might touch the aorta. This would impair mobility and could cause stenosis or regurgitation. Therefore an outer cage was added to ensure freedom of ball motion. The ball is almost isobaric to blood (specific gravity—1.1499) so that it moves with minimal resistance in response to changes in the blood flow. For example, at a pressure of 80 mm. Hg acting downward on top of the ball, it will be displaced upward by a pressure change of 0.12 mm. Hg. Expressed in general terms, at this pressure level, opening requires only a 0.15 per cent pressure increment.

The valve is so constructed that it can be firmly anchored by Surgaloy[*] and covered by silk sutures in Ivalon[†] or Teflon backing. This, when cut into the shape indicated (Fig. 5), can be moved into position (Fig. 6) away from the ostia of the coronary arteries and yet provide an effective outflow tract. Further coronary clearance is gained by creating a small enlargement of the sinus of valsalva. The fundus of the noncoronary bearing cusp is excised (Figs. 6 and 7).

VALVE TESTING

Valves must not only be tested for fatigue, as discussed earlier, but for pulse contour, competence, resistance to flow, and trauma to formed blood elements.

A pulse duplicator has been constructed to study valve competence (Fig. 8). This mechanical device is composed of nine essential components. Part I is the actuator (Fig. 8, *6*) which contains a piston compressor that can vary its volume, rate, and duration of systole and diastole. Control is through the box (Fig. 8, *7*). The fluid is delivered into a rigid chamber corresponding to the ventricle (Fig. 8, *8*). From the rigid tube, a side-arm (Fig. 8, *9*) is provided where pressure contours can be recorded. The testing chamber (Fig. 8, *1*) contains the valve. Beyond the chamber housing for the valve is an elastic tubing that corresponds to the aorta (Fig. 8, *2*). Systemic pressure recording can be made at another side-arm (Fig. 8, *3*) which corresponds to the aortic arch. The character and degree of peripheral resistance can be altered by the position and degree of closure of a bar clamp (Fig. 8, *4*). Beyond the resistance clamp, the blood or circulating solution is returned to a reservoir (Fig. 8, *5*) in which there is a break in continuity so that the "arterial" system is interrupted to form a "venous" return.

This apparatus has been used in testing competence and pulse pressure contours for various types of valves. The caged-ball valve is competent when tested on this apparatus and produces pressure contours similar to those in the human being. These findings have been confirmed in our clinical experience (Fig. 9).

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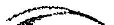
[*] Surgaloy—American Cyanamid Co., Danbury, Conn.
[†] Ivalon—Clay-Adams, Inc., New York 10, N. Y.



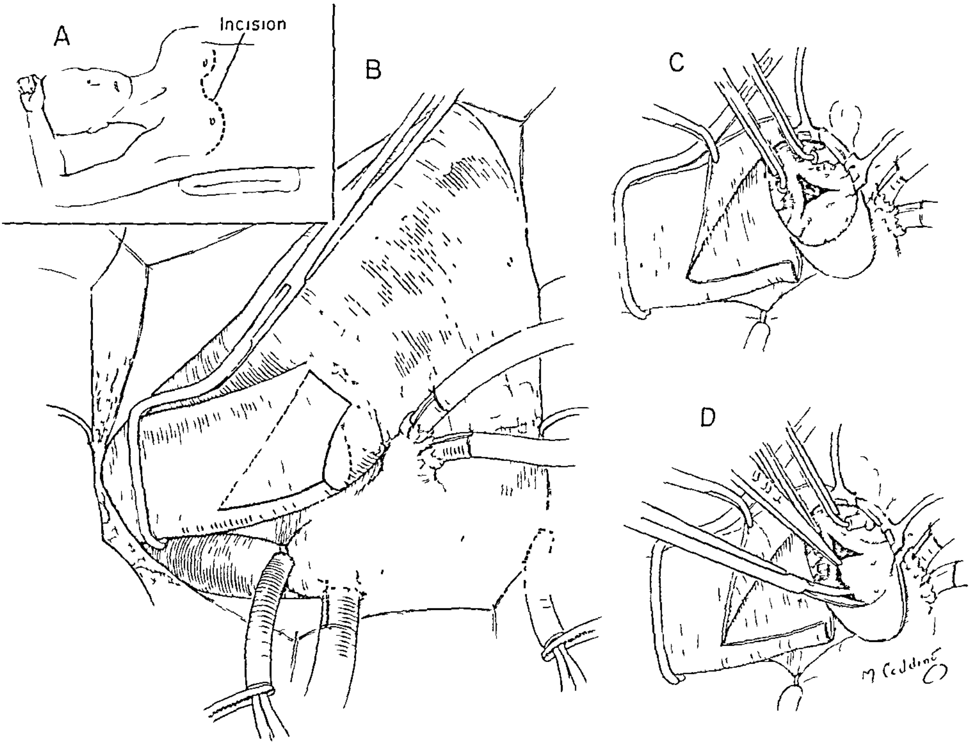


Fig. 6.—Technique of exposure of aortic valve.

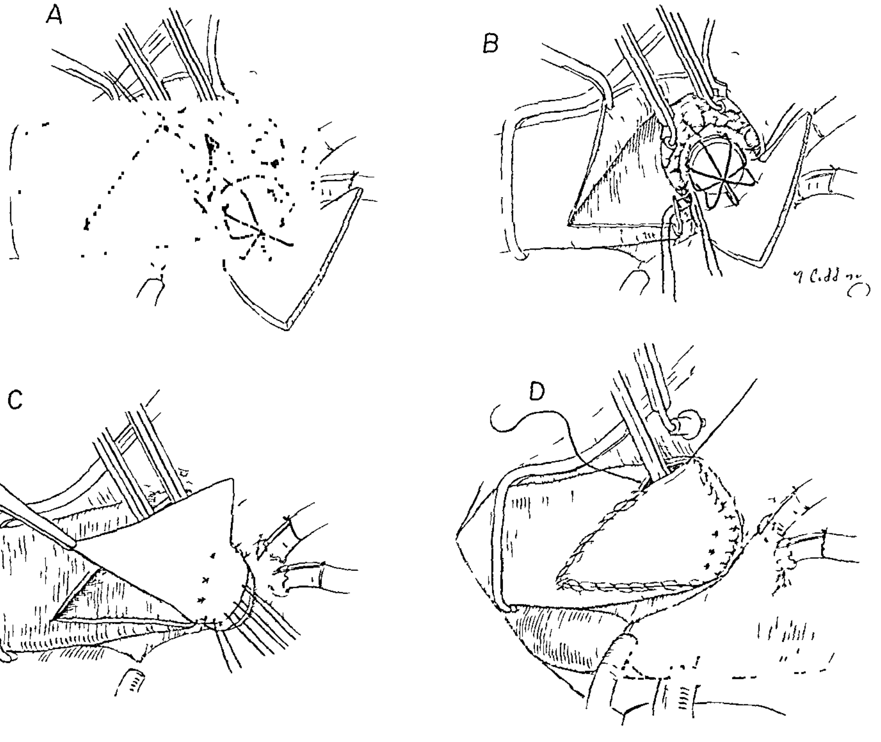


Fig. 7.—Technique of insertion of caged-ball valve

Flow resistance through a valve is of prime importance. Continuous flow studies oversimplify the problem. However, at 10 L./min. the caged-ball valve offered no gradient. At 20 L./min., the gradient was 25 mm. Hg. Twenty liters a minute continuous flow would correspond to an average flow of 10 L./min. output at a pulse rate of 120, where time in systole equals diastole.

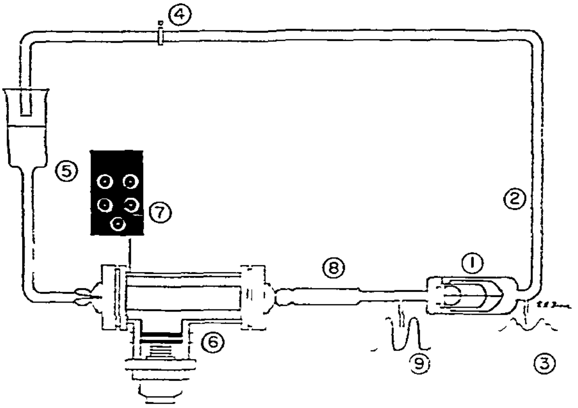


Fig. 8.—Schematic diagram of pulse duplicating system

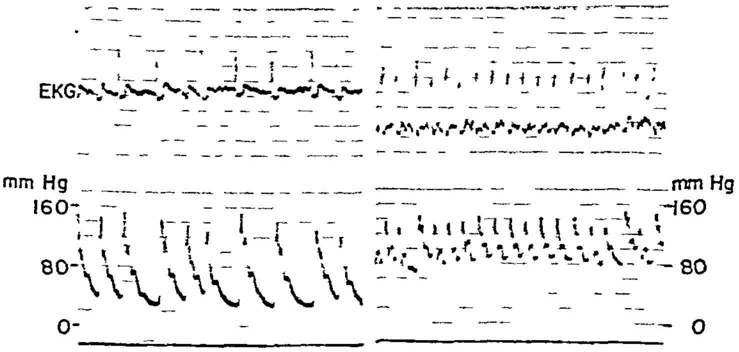


Fig 9.—Pulse contour (Case 3) before and after surgery.

The caged-ball valve does not seem to be destructive to blood elements either experimentally or clinically.

Apparently the caged-ball valve is atraumatic, competent, enduring, quiet, offers little resistance to flow, and produces normal pulse contours.

CLINICAL USE OF THE CAGED-BALL VALVE

Our small clinical experience can be best presented in the form of case abstracts, omitting much significant clinical, pathologic, hemodynamic, hematologic, and metabolic data. After the case presentations a review of the dominant problems of the whole group clarifies the evolution of this technique.

A. *Case Reports.*—

CASE 1.—D. L. (PBBH No. 4P339), a 27-year-old man, had rheumatic fever at the age of 14. This was followed by evidence of severe aortic insufficiency accompanied by cardiomegaly, exercise limitation, and rare episodes of transient blindness. During the 2 years prior to hospitalization he had three episodes of congestive failure followed by increasing dyspnea, angina, paroxysmal nocturnal dyspnea, fatigue, and orthopnea. At the time of admission he was completely incapacitated in spite of intensive medical therapy.

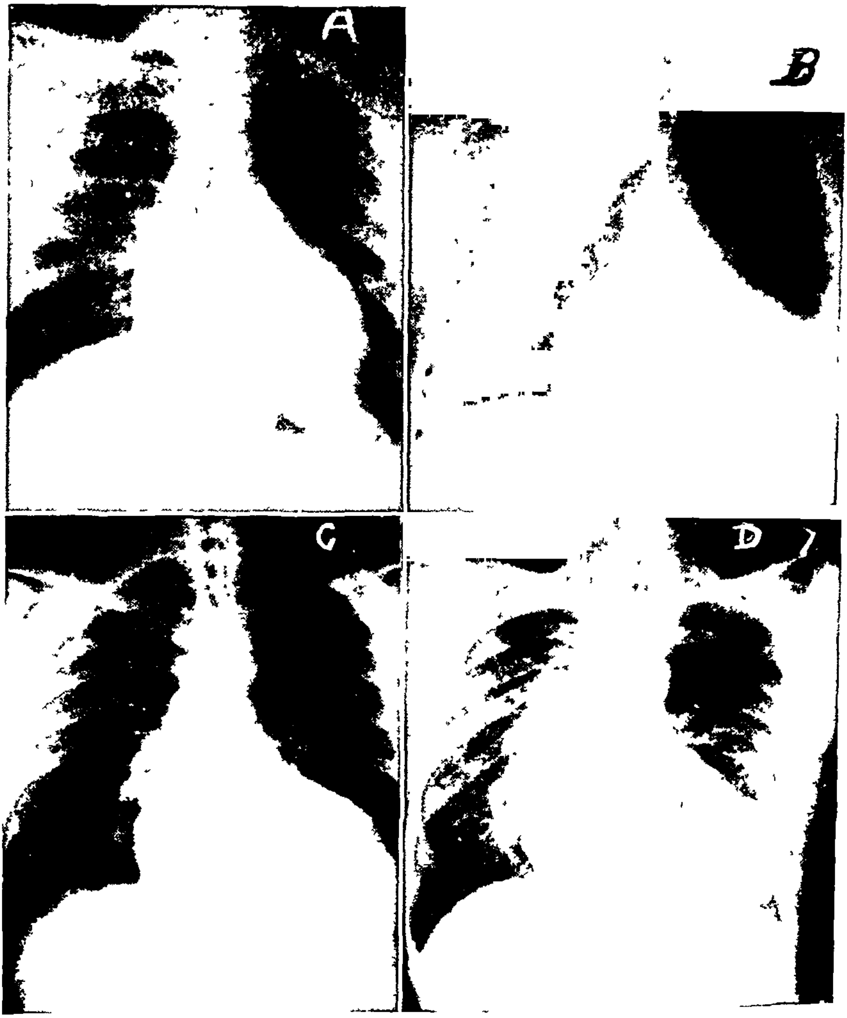


Fig. 10.—Posteroanterior roentgenograms of patients who died during insertion of prosthetic valve.

Physical examination: The blood pressure was 210/0 mm. Hg. The heart was enlarged to the anterior axillary line. There was a diffuse apical impulse and a left ventricular heave. There was a systolic ejection click and an accentuated pulmonary second sound. There were Grade 2 systolic and Grade 3 diastolic aortic murmurs. Grade 2 presystolic rumble was present at the apex. The liver was palpated two fingerbreadths below the right costal margin. There was no peripheral edema.

Roentgenograms (Fig. 10, *A*) and fluoroscopy revealed cardiomegaly with marked left ventricular enlargement. No calcification of the aortic valve was seen. The rocking beat of aortic insufficiency was no longer present. This was interpreted as an ominous sign.

Electrocardiogram showed normal sinus rhythm, left bundle branch block, and left ventricular hypertrophy.

Hospital course: He developed bouts of supraventricular tachycardia and angina decubitus persisted. A low-grade fever led to the diagnosis of and treatment for subacute bacterial endocarditis, although blood cultures were negative. He lost 3 kilograms in weight on a diuretic program.

At operation on bypass the patient was cooled to 26° C. with the Brown-Harrison heat exchanger. Ventricular fibrillation occurred at 28.4° C. and the aorta was cross-clamped and opened at once. Hypothermic arrest was brought about using intracardiac and extracardiac Ringer's solution at 4° C. The aorta was occluded for a total of 63 minutes while the caged-ball valve was inserted (see Figs. 6 and 7). With the resumption of coronary flow at release of the aortic clamp, transient defibrillation was accomplished but marked dilatation occurred followed by failure and again by fibrillation. In the dilated ventricle, defibrillation was impossible. The cannula had been placed in the left auricle and did not decompress the ventricle adequately.

Postmortem examination: The empty heart weighed 750 grams. There was right and left ventricular dilatation and hypertrophy and a partial occlusion of the anterior descending branch of the left coronary artery by an atheromatous plaque.

CASE 2.—M. R. (PBBH No. 4P565) is a 32-year-old woman without a history of rheumatic fever. A murmur was first heard at age 9 and since then she noted fatigue and slight exertional dyspnea. At 18 her only pregnancy was complicated by glomerulonephritis. At 26 she developed increasing fatigue, dyspnea, and transient left anterior chest pain. There were "weak spells" but no true syncope. Three years later, in the presence of progressive dyspnea, paroxysmal nocturnal dyspnea, and occasional ankle edema, she was admitted to another hospital for cardiac evaluation. Data from percutaneous dorsal catheterization of the left heart were incomplete because of syncope and shock. On the basis of clinical evaluation and available catheter data, transaortic valvuloplasty was performed. Stenosis of approximately 1.2 sq. cm. with regurgitation was partially corrected by finger fracture valvuloplasty. Transient improvement was followed by progressive limitation from dyspnea, orthopnea, and peripheral edema. At the time she was admitted for re-evaluation, she had dyspnea on less than one flight of stairs and angina decubitus.

Physical examination: The lungs were clear and the liver edge palpable at the costal margin. The blood pressure was 150/80 mm. Hg and the heart was in normal sinus rhythm. A left ventricular impulse was felt in the anterior axillary line. Grade 3 aortic systolic and diastolic and Grade 1 mitral diastolic murmurs were present. The aortic second sound was diminished.

Roentgenograms (Fig. 11, *A* and *B*) and fluoroscopy demonstrated moderate left ventricular enlargement and no calcification of the aortic valve. A definite rocking beat was present. The transverse cardiac diameter was within accepted normal limits.

The electrocardiogram showed normal sinus rhythm and left ventricular hypertrophy.

At transseptal cardiac catheterization, no gradients were noted across the aortic or mitral valves at a flow of 5.1 L./min. The dye dilution curves indicated regurgitation. The left ventricular end-diastolic pressure was 12 mm. Hg. Mild oxygen desaturation (89 per cent) was present in the sedated basal state.

Ventilatory studies and laboratory analyses, for serum electrolytes and blood constituents, were within normal limits.

Hospital course: Intensive medical therapy resulted in a weight loss from 69 to 66 kilograms. At *open operation*, on bypass, there was free relative aortic insufficiency from backward and downward displacement of the neutral cusp. The right coronary cusp was torn through its lateral commissure to the base of the fundus. The leaflet complex could prolapse in diastole. Using a heat exchanger, body temperature was lowered. At 29° C. the heart went into ventricular fibrillation. During the ensuing 64 minutes of total bypass, at flow rates averaging 3,600 c.c./min., the patient's temperature remained at 28° C. The left ventricle was decompressed through a No. 38 plastic catheter. Adequate bilateral coronary perfusion was not attained. After the caged-ball valve had been placed (see Figs. 6 and 7) and as the patient was being rewarmed, the heart spontaneously reverted to a regular rhythm at 32° C. Assisted circulation was continued for an additional 20 minutes. Thereafter, she maintained an adequate cardiac output with good systemic pressures. Aortic pulse tracings before operation were characteristic of aortic insufficiency and were normal after the valve was placed. The roentgenogram after operation shows the valve in place (Fig. 11, C and D).

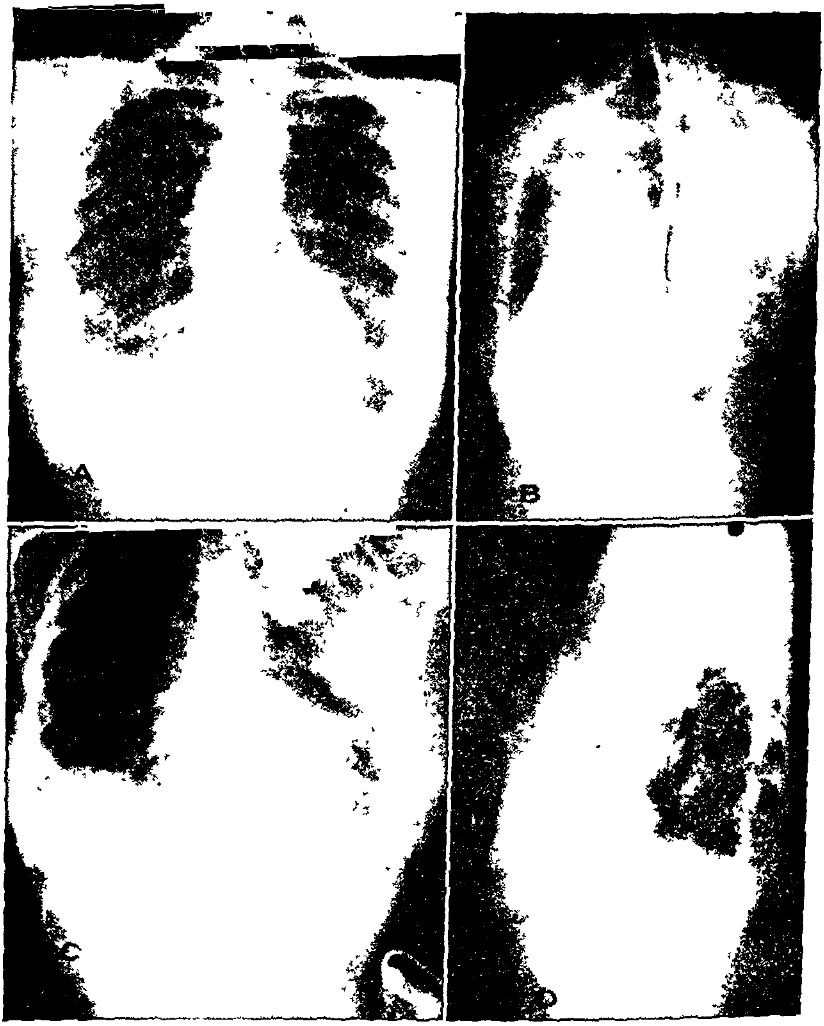


Fig. 11—Roentgenograms of patient who survived insertion of prosthetic valve.

During the first 3 postoperative days, the patient had premature ventricular beats and idioventricular foci alternating with sinus tachycardia. Adjustment of the digitalis dosage corrected this situation. During the ensuing 10 days she ran a low-grade fever to 102.4° F. and broad spectrum antibiotics were given. Blood cultures were negative. The remainder of her course was uneventful. She has remained on digitalis and a low sodium diet. Diuretics have not been necessary. Her condition is entirely satisfactory at an essentially normal activity level.

In spite of inadequate coronary perfusion this patient was successfully resuscitated. Survival appears to be correlated with a compact nondilated left ventricle.

CASE 3.—R. H. (PBBH No. 4P572), a 28 year old man, had rheumatic fever at the age of 11. He was asymptomatic until age 24 when he developed acute dyspnea. Three months prior to this admission, the dyspnea and fatigue became refractory to medical therapy. At this time he was observed fluoroscopically and the cardiac and aortic activity were exaggerated, characteristic of aortic insufficiency. There was no angina or syncope.

Physical examination: The blood pressure was 160/60 mm. Hg. He had Corrigan pulse. There were expiratory râles. The point of maximal impulse was in the anterior axillary line and was accompanied by a characteristic left ventricular heave. The right ventricular contraction was not prominent. The aortic second sound was normal but the pulmonic sound was accentuated. At the base there was a Grade 2 rough systolic ejection murmur and a Grade 4 diastolic diminuendo murmur along the left sternal border. At the apex there was a Grade 3 pansystolic murmur and a Grade 2 diastolic rumble with an opening snap. In the tricuspid area there was a Grade 3 diffuse rough pansystolic murmur that was louder during inspiration. The liver edge was palpated two fingerbreadths below the right costal margin. There was no edema.

X-ray studies (Fig. 10, *B*) and fluoroscopy revealed considerable enlargement of the left ventricle (3+), right ventricle (2+), and left auricle. The transverse diameter was increased 34 per cent above the predicted normal and the pulmonary vascular bed was congested. There was no calcification and no rocking motion (although this had been vigorous).

Electrocardiogram revealed auricular fibrillation, intraventricular conduction defect, and left ventricular hypertrophy.

Combined heart catheterization revealed a total cardiac output of 6.2 L./min./M.^{2} with a regurgitant flow estimated at 2.91 L./min./M.^{2} or 47 per cent of total cardiac output. Pressures were elevated in all chambers of the right heart. Pulmonary artery pressure rose from a resting level of 61/30 to 110/58 mm. Hg with exercise indicating left ventricular failure. Left ventricular pressures were not obtained.

Hospital course: On bed rest and a full medical program, the patient lost 3 kilograms of fluid. At open operation, a caged ball valve was inserted by the technique described. The patient was cooled to 28° C. Ventricular fibrillation occurred at 29° C. There was inadequate coronary perfusion during 56 minutes of aortic occlusion. The tenth defibrillating shock of 280 volts at 1/20 second restored regular rhythm and effective left ventricular contractions followed. Partial bypass was continued for an hour after release of the aortic clamp. After operation, the temperature rose to 105° F. and there was a tachycardia of 130 on the second postoperative day. His temperature was lowered to 95° to 96° F. and vasopressors were needed on the third day. The patient remained lucid and cooperative under these conditions. Urinary output ranged from 400 to 950 c.c. daily and cardiac rate varied from 130 to 160 per minute. The rhythm showed frequent changes from a supraventricular tachycardia, possibly flutter, to auricular fibrillation that constituted a problem in management. There was mild gastric bleeding. *Staphylococcus aureus* was cultured from the tracheobronchial tree but blood cultures were negative. On the seventh postoperative day, hypothermia and vasopressors were discontinued because of improvement but, as on previous occasions, each elevation of temperature was associated with ventricular tachycardia. On the eighth postoperative day the patient developed hypotension, ventricular tachycardia and fibrillation, and died.

Postmortem examination revealed that the prosthetic valve was well placed with patent coronary ostia. There were massive old and recent myocardial infarctions of the apex of the left ventricle. The empty heart weighed 980 grams. Although there was no evidence of coagulation necrosis it is felt that the ten electrical shocks contributed to the obvious old and recent massive infarctions as a cause of death.

Case 4—L L (PBBH No. 4P675), a 32 year old man, had had scarlet fever at the age of 9. He was discharged from the Army because of rheumatic heart disease Acute nephritis and polyarthritis occurred at 27 He then remained well until one month prior to hospitalization when he developed left ventricular failure, cough, dyspnea, orthopnea, pulmonary edema, and exertional precordial pain radiating down both arms

Physical examination: Bisferiens carotid pulses and pistol shot femoral pulses were present The lungs were clear. The liver edge was palpated two fingerbreadths below the costal margin The blood pressure was 145/40 mm Hg and the heart was in normal sinus rhythm A diffuse left ventricular heave was felt in the 6th interspace at the anterior axillary line Grade 3 aortic systolic and diastolic murmurs were heard

Roentgenograms (Fig 10, C) and fluoroscopy revealed aortic valve calcification and marked left ventricular enlargement A definite rocking beat was present The transverse cardiac diameter was 65 per cent above predicted normal

The electrocardiogram showed normal sinus rhythm, left auricular enlargement, left ventricular hypertrophy, and an intraventricular block.

At transseptal cardiac catheterization there was no mitral or aortic gradient at a cardiac output of 4.3 liters The left ventricular end diastolic pressure was 29 mm Hg, indicating left ventricular failure Dye dilution curves indicated marked regurgitation

Hospital course· Diuretics produced a weight loss of 4 8 kilograms At open operation on bypass, free aortic regurgitation was found to be due to enlargement of the aortic base and shift of the mitral cusp There was slight calcification and commissural fusion The temperature was reduced to 26° C with a heat exchanger Ventricular fibrillation occurred at 28 5° C. Both coronary arteries were perfused at approximately 120 c c per minute total flow The left ventricle was vented through a No 38 plastic catheter Placement of the caged ball valve required 60 minutes There were 22 ineffective shocks at 280 volts of 1/20 of a second Standstill was ultimately produced after giving 2 Gm of quinidine and a shock of 130 volts for 3 5 seconds The inability to place this massive ventricle in standstill with standard equipment clarified the need for more powerful defibrillators

At *autopsy* the valve was well placed The empty heart weighed 1,120 grams and was dilated There was an old myocardial infarction at the apex of the left ventricle No evidence of coagulation type necrosis was found

Case 5—N R (PBBH No 4P740), a 49 year old man, was first known to have heart disease at the age of 26, when a murmur was heard He gave no history of acute rheumatic fever His first symptom, an isolated episode of syncope, occurred at the age of 34 after exertion Exertional dyspnea developed at 41 years of age and became progressive Two years before admission he had transient right sided weakness and aphasia This was treated with anticoagulants Marked deterioration began a year prior to hospitalization An episode of fever and congestive failure suggested subacute bacterial endocarditis Penicillin was given, although an organism was never isolated On admission, he was dyspneic after climbing one half flight of stairs and had orthopnea He did not have angina, hemoptysis, peripheral edema, or further episodes of syncope A vigorous medical and diuretic program had resulted in a weight loss of 5 kilograms during the preceding 2 weeks

Physical examination Bisferiens carotid pulses and pistol shot femoral pulses were present The blood pressure was 110/60 mm Hg and the heart was in normal sinus rhythm There were fine moist râles at bases of both lungs There was a moderate dorsal kyphoscoliosis The liver edge was palpated three fingerbreadths below the costal margin A diffuse left ventricular heave was felt in the sixth interspace outside the anterior axillary line A Grade 4 aortic systolic murmur and a Grade 2 aortic diastolic murmur were heard

Roentgenograms (Fig 10, D) and fluoroscopy revealed marked left ventricular enlargement, a tortuous ascending aorta, and heavy aortic valve calcification A rocking beat was not present The transverse cardiac diameter was 63 per cent above predicted normal

The electrocardiogram showed normal sinus rhythm with left ventricular hypertrophy, first degree left bundle branch block, and first degree heart block

At transseptal cardiac catheterization there was a 29 mm Hg mean systolic gradient across the aortic valve at a flow of 3 7 L /min Peak left ventricular systolic pressure was 141 mm Hg and the end diastolic was 31 mm Hg, indicating left ventricular failure Dye dilution curves indicated marked regurgitation

Ventilatory studies showed a moderate reduction in all values. vital capacity, 2.34 L (55 per cent of predicted); maximum breathing capacity, 78 L (69 per cent of predicted); and timed vital capacity, 73 per cent in one second

Serum electrolytes and blood constituents were within accepted normal limits

Hospital course After 22 days of intensive medical therapy, the liver edge had receded to the costal margin, the lungs cleared, and the patient lost 6 more kilograms of weight At open operation, on bypass, aortic insufficiency was due to contraction of all leaflets and a perforation in the base of the left coronary cusp The right and left coronary bearing cusps were fused and heavily calcified The caged ball valve was inserted as illustrated (see Figs 6 and 7). Bilateral coronary perfusion averaged more than 150 c c. per minute total flow at normal temperatures A single reservoir made an estimate of individual artery perfusion impossible. The aorta was cross clamped for approximately 60 minutes but at 35 minutes the ventricle fibrillated During bypass, massive bleeding developed from all incised surfaces This necessitated rapid replacement transfusions Ventricular fibrillation was successfully converted to arrest by one shock of 250 volts at 0 15 second, but a sustained orderly contraction was not restored Continued bleeding necessitated 43 units of citrated blood within 2 hours Despite continued assisted circulation, resuscitative efforts failed It was never possible to take this patient off of extracorporeal circulation

In spite of apparently adequate coronary perfusion, ventricular fibrillation developed making evident the necessity for measured individual coronary artery perfusion This patient s uncontrollable bleeding problem, requiring replacement transfusions with ACD blood, may have imposed additional metabolic burdens and complicated the resuscitative effort, even though there was the usual calcium coverage

B *Discussion of Cases.—*

In the first patient the immediate problem was inadequate venting or decompression of the left ventricle. In previous open-heart surgery, left auricle venting had been sufficient However, with the valve in place, a reverse transaortic gradient was not maintained and the valve became incompetent Pressure from the aorta was transmitted directly to the dilated left ventricle This afforded hydraulic multiplication of the pump pressure so that the ventricle violently expanded The venting cannula was then rearranged in subsequent procedures so as to pass through the wall of the left auricle and the mitral valve, directly into the left ventricle. Decompression could be controlled by aspiration from the roller pump or by gravity.

The second patient was cooled to 28° C Partial coronary perfusion with imperfect apparatus was carried out There was good left ventricular decompression through a No 38 Bardic catheter * The heart went into ventricular fibrillation at 29° C Following valve insertion, the heart spontaneously reverted to a regular rhythm as the patient's temperature rose to 32° C. She has done extremely well since Her roentgenograms are shown in Fig 11 She does not have an extremely large ventricle. This may account for the success

The third patient had a much larger ventricle (Fig 10, *B*), both dilated and hypertrophied In spite of adequate decompression of the left ventricle.

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*C R Bard Inc Summit N J

the heart fibrillated and defibrillation was not effective until the tenth shock of 280 volts at 1/20 sec. Thereafter he could maintain an effective blood pressure only with vasopressors and at a body temperature of 34° C. Whenever the temperature was brought to normothermic levels, tachycardia became excessive and ventricular irritability increased. After 7 days of such hypothermia and in the presence of a gradual increase in pulmonary infection yet general improvement, the patient was warmed. This was found incompatible with his heart function. He had cardiac irritability, ventricular fibrillation, and succumbed on the eighth postoperative day. His difficulty at operation stemmed initially from ventricular fibrillation, then secondarily to the inability to defibrillate promptly. It was thought that coagulation damage had been caused by the multiple shocks but evidence on microscópic examination is lacking. He did, however, show a massive old and recent apical myocardial infarction. The old lesion antedated the operation. It is interesting and perhaps significant to know that a vigorous left ventricle and markedly active aortic arch had been observed in previous years, but on admission to the hospital the arch and ventricle were quiet. Presumably the infarction and failure accounted for this.

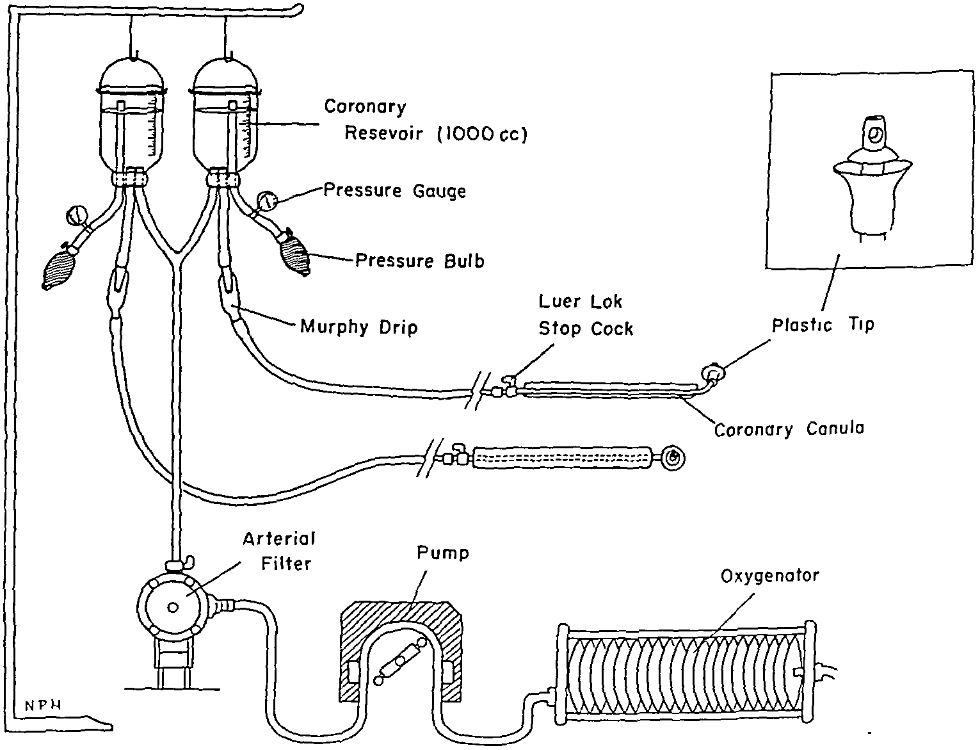

Fig. 12.—Coronary perfusion apparatus for separate perfusion of coronary arteries.

The fourth patient had a still larger ventricle (Fig. 10, *C*) although in a better state of compensation as attested by the end-diastolic pressure and by the vigor of the pulsation. This caged-ball valve was placed without difficulty.

Decompression was good but ventricular fibrillation refractory. Two hundred and eighty volts at 1/20 second did not cause standstill. It was not until the twenty-third shock, with another defibrillator delivering 130 volts for 3½ seconds, that this ventricle was arrested. However, a satisfactory beat was never restored. Although evidence of coagulation necrosis is not clear in the microscopic specimens of heart muscle, we find it difficult to believe that the 22 ineffective shocks of 280 volts were not related to this death. This patient demonstrated the necessity for better coronary perfusion and a more powerful defibrillator that could produce standstill in such a massive ventricle. Apparently these ventricles may have been so large as to render ordinary defibrillators inadequate.

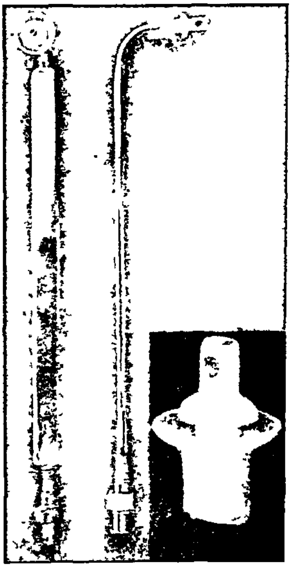

Fig 13.—Handles and tips of the coronary cannulas

The coronary perfusion equipment had a common trunk of origin from the reservoir, so we could not tell how much of the blood was being delivered to each coronary artery. Furthermore we had not fully appreciated the importance of perfusing both coronary arteries. Contrary to the popular impression, Schlesinger[21] showed that in all but 18 per cent of people the right coronary artery supplies a significant part of the left ventricle or septum. This pointed up the necessity for effective perfusion of both arteries and independent reservoirs so that the flow to each could be verified.

The improved coronary perfusion apparatus (Fig. 12), handles and tips (Fig. 13), were then devised.* A defibrillator with a set time interval of 0.15 second and a variable manual time control delivering up to 250 volts was then obtained.†

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*Manufactured by Davol Company, Providence, R. I.
†Electrodyne Company, Norwood, Mass.

In the fifth patient, the incision at the base of the aorta was extended to afford better exposure and perfusion of the coronary arteries (see Fig. 6). Even so, the heart did fibrillate. More effective shock brought this large ventricle into standstill followed by a transient organized beat, but this was neither effective nor sustained. However, this patient presumably died because of a bleeding problem. Forty-three citrated blood transfusions were given in approximately 2 hours, but the bleeding became steadily more profuse from all incised surfaces. This may have contributed to or caused the failure. Excess citrate or the alkalosis resulting from its oxidation are both hazardous in the digitalized cardiac surgical patient, despite the measures commonly used to prevent citrate "toxicity."[22]

COMMENT

At this point it is clear that this valve and the technique of placing it do not constitute a solution to the problem of aortic insufficiency in patients who have markedly dilated left ventricles in failure. The roentgenograms (Fig. 11) indicate that the only survivor with a complete prosthesis was a woman who had a smaller ventricle than those who died (Fig. 10).

We plan to continue this effort. The combination of better coronary perfusion, perhaps hypothermia at 32° C., improved left ventricle decompression, and adequate defibrillating apparatus may allow the necessary time (50 to 70 minutes) for valve installation.

So far we have not been able to use our synchronized pulsatile pump[23] effectively in this situation. It has been impossible to synchronize the pump inflow with the disorderly ventricular complex. Possibly this apparatus may be rendered useful by changing the activating impulse from the R wave of the electrocardiogram to the alterations in aortic pulse pressure.

This group of patients threatens to remain beyond surgical correction. On the other hand, if they can be salvaged by a suitable prosthesis, we can apply this knowledge to the treatment of combined aortic stenosis and regurgitation and, later, to pure stenosis. Better valves than the caged-ball valve may well be developed, but the site and technique of insertion described here seem valid and the testing equipment may continue to be useful.

SUMMARY

1. Anatomic and pathologic features of aortic insufficiency are reviewed.

2. The rationale for nonflexible cusp extension on the neutral flexible cusp is presented.

3. The clinical experience with 4 patients who had nonflexible prosthetic cusp extension in aortic insufficiency is mentioned.

4. The requirements for testing total aortic valve prostheses as to competence, resistance, fatigue, and trauma to blood elements are mentioned and certain testing equipment is described.

5. Special problems of decompressing (sumping) the left ventricle with reference to mural tension and ventricular dilatation are pointed out.

6. Shortcomings in conventional coronary perfusion equipment and defibrillation are considered and better equipment is described.

7. Consideration is given the problems encountered in four unsuccessful operations involving total aortic valve insertion in patients with free insufficiency with dilated left ventricles in failure.

8. A case of successful total aortic valve replacement with a caged-ball valve is reported. Future possibilities of this technique are considered.

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REFERENCES

1. Lillehei, C. W., DeWall, R. A., Gott, V. L., and Varco, R. L.: The Direct Vision Correction of Calcific Aortic Stenosis by Means of a Pump Oxygenator and Retrograde Coronary Sinus Perfusion, Dis. Chest 30: 123-132, 1956.
2. Lillehei, C. W., Gott, V. L., DeWall, R. A., and Varco, R. L.: The Surgical Treatment of Stenotic or Regurgitant Lesions of the Mitral and Aortic Valves by Direct Vision Utilizing a Pump Oxygenator, J. THORACIC SURG. 35: 154-189, 1958.
3. Bailey, C. P.: Discussion of paper by Harken et al.[4]
4. Harken, D. E., Black, H., Taylor, W. J., Thrower, W. B., and Soroff, H. S.: The Surgical Correction of Calcific Aortic Stenosis in Adults, J. THORACIC SURG. 36: 759-776, 1958.
5. Harken, D. E., Black, H., Taylor, W. J., Thrower, W. B., Soroff, H. S., and Bush, V.: The Surgical Correction of Calcific Aortic Stenosis in Adults: Technique of Transaortic Valvuloplasty, Cardiology 4: 135-146, 1959.
6. Brock, R.: Surgical Treatment of Aortic Stenosis, Brit. M. J. 1: 1019-1028, 1957.
7. Glover, R. P., and Gadboys, H. L.: Seven Years' Experience With Transventricular Aortic Commissurotomy, J. THORACIC SURG. 36: 839-856, 1958.
8. Swan, H., Wilkinson, R. H., and Blount, S. G., Jr.: Visual Repair of Congenital Aortic Stenosis During Hypothermia, J. THORACIC SURG. 35: 139, 1958.
9. Morrow, A. G.: Personal communication regarding the open correction of aortic stenosis under hypothermia.
10. Wells, R. E., Taylor, W. J., Black, H., and Harken, D. E.: Pulmonary Function in the Selection of Patients for Open Heart Surgery, Dis. Chest. (In press.)
11. Harken, D. E., Black, H., Taylor, W. J., Thrower, W. B., and Ellis, L. B.: Reoperation for Mitral Stenosis: A Discussion of Postoperative Deterioration and Methods of Improving Initial and Secondary Operations, Circulation. (In press.)
12. Taylor, W. J., Thrower, W. B., Black, H., and Harken, D. E.: The Surgical Correction of Aortic Insufficiency by Circumclusion, J. THORACIC SURG. 35: 192-205, 230-231, 1958.
13. Garamella, J. J., Andersen, J. G., and Oropeza, R.: The Surgical Treatment of Aortic Insufficiency by Open Plastic Revision of the Tricuspid Aortic Valve to a Bicuspid Valve, Surg. Gynec. & Obst. 106: 679-686, 1958.
14. Garamella, J. J., Andersen, J. G., Oropeza, R., Veloso, A., and Naidu, R.: The Surgical Treatment of Aorta Insufficiency by Conversion of Tricuspid Aortic Valve to a Bicuspid Valve, J. THORACIC SURG. 37: 177, 1959.
15. Bailey, C. P., and Zimmerman, J.: The Surgical Correction of Aortic Regurgitation—Bicuspid Conversion, Am. J. Cardiol. 3: 6-21, 1959.
16. Muller, W. H., Jr., Warren, W. D., Dammann, J. F., Jr., Beckwith, J. R., and Wood, J. E., Jr.: Surgical Relief of Aortic Insufficiency by Direct Operation on the Aortic Valve, Circulation 21: 587-597, 1960.
17. Bahnson, H.: Personal communication.
18. Harken, D. E., Black, H., Ellis, L. B., and Dexter, L.: The Surgical Correction of Mitral Insufficiency, J. THORACIC SURG. 28: 604-627, 1954.

19. Hufnagel, C. A., Harvey, W. P., Rabil, P. J., and McDermott, R. F.: Surgical Correction of Aortic Insufficiency, Surgery 35: 673, 1954.
20. Hufnagel, C. A., Vilkgas, P. D., and Nahas, H.: Experience With New Types of Aortic Valvular Prostheses, Ann. Surg. 147: 636-645, 1958.
21. Schlesinger, M. J.: Relation of Anatomic Pattern to Pathological Conditions of the Coronary Arteries, Arch. Path. 30: 403-415, 1940.
22. Moore, F. D.: Metabolic Care of the Surgical Patient, Philadelphia, 1959, W. B. Saunders Company.
23. Clauss, R. H., Birtwell, W. C., Albertal, G. A., Lunzer, S., Taylor, W. J., Fosberg, A. M., and Harken, D. E.: Assisted Circulation. I: The Arterial Counter Pulsator, J. THORACIC SURG. (In press.)

(For Discussion, see page 799.)

SURGICAL TREATMENT OF VENTRICULAR SEPTAL DEFECT

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PATIENTS with severe pulmonary hypertension and infants pose the greatest challenges in the surgical treatment of ventricular septal defect. In other circumstances good results have been obtained with relative ease. The experience here reported indicates that, by application of proper techniques, a low hospital mortality can be achieved in infants as well as in patients with most types of ventricular septal defect with severe pulmonary hypertension.

MATERIAL

All 320 cases in which ventricular septal defect was treated on one surgical service at the Mayo Clinic prior to April 1, 1960, are included in this study. Results in the total group operated upon in this clinic are similar, but their inclusion would have introduced additional variations in technique and management, making analysis more difficult. The history, operative reports, chest roentgenograms, electrocardiograms, and necropsy findings from each case were reviewed individually.

Cases of tetralogy of Fallot, as previously defined,[1] have not been included. Likewise, cases in which the interventricular communications were part of the malformations known as complete common atrioventricular canal, single ventricle, origin of both vessels from right ventricle, infundibular pulmonary stenosis with tiny ventricular septal defect, or corrected transposition of the great vessels have been excluded.

Associated malformations other than pulmonary stenosis are listed in Table I. Pulmonary stenosis is not included in the table, since patients with this entity are categorized separately in the section on results. The lesions indicated were corrected at the time of repair without complication, except for severe mitral and aortic valvular insufficiency and the combination of patent ductus arteriosus and coarctation of the aorta. These also will be considered separately

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under results. The shunt across a high ventricular septal defect was recognized as being wholly or in part into the right atrium in 20 cases. In 15 of these, pulmonary hypertension was only mild or moderate.

TABLE. I. CERTAIN ASSOCIATED CARDIOVASCULAR ANOMALIES IN 320 CASES WITH OPERATION FOR VENTRICULAR SEPTAL DEFECT

ANOMALIES	CASES
Repaired at Time of VSD Repair	
Atrial septal defect	20
Patent ductus arteriosus	16
Aortic-pulmonary fistula	1
Aortic-valve insufficiency	5
Mitral-valve lesions	
Stenosis	1
Insufficiency,* severe	5
Coarctation of aorta and patent ductus arteriosus	4
Not Repaired at Time of VSD Repair	
Aortic-valve deformity with minimal stenosis	3
Mitral-valve insufficiency,* mild	9
Anomalous right coronary artery supplying left anterior descending artery†	4
Coarctation of aorta	4
Persistent left superior vena cava	22
Stenosis of right or left pulmonary artery	2
Absence of left pulmonary artery	1
Right aortic arch	2

*Exclusive of endocardial-cushion defects.
†Preserved without damage in all cases.

Patients were categorized as having mild pulmonary hypertension when pulmonary-artery systolic pressure was 45 per cent or less of systemic-artery systolic pressure, moderate pulmonary hypertension when it was between 45 per cent and 75 per cent of systemic-artery pressure, and severe pulmonary hypertension when it was 75 per cent or more of systemic-artery pressure. Patients with severe pulmonary-artery hypertension were further divided into those whose pulmonary/systemic blood flow ratios were high (1.8 or more), moderately elevated (1.3 to 1.8), and low (less than 1.3). When complete data had been obtained by cardiac catheterization without anesthesia, they were used for classification of the case. In some instances, particularly among small children, the conditions existing during cardiac catheterization result in hypoventilation. Values for pulmonary-artery pressure then tend to be abnormally high, and those for pulmonary/systemic flow abnormally low. This can make a patient appear less favorable for operation than in fact he is. In such instances, the patient was categorized according to the clinical data and the pressure measurements which were made routinely at the time of surgery. These findings alone were utilized in cases where preoperative catheterization data were not available. The clinical data were derived from physical examination, the chest roentgenogram, and the electrocardiogram. For the most part, criteria used for categorization of the patient on the basis of these data have been validated previously.[2-6]

Defects immediately below the aortic leaflets are called *high ventricular septal defects.* Although they vary considerably in their exact relation to the tricuspid-valve leaflets and in their size, basically similar techniques of repair can be used for all. With some high defects, a small muscular defect was associated. A special category of high defects are those immediately beneath the commissure between right and left aortic cusps, and thus *immediately beneath the pulmonary valve.* Certain defects not immediately beneath the aortic leaflets are triangular, with their cephalad margin formed by the tricuspid valve. Frequently some of the chordae tendineae of this valve are attached to a papillary muscle within the left ventricle. Very often there is a cleft in the anterior mitral leaflet alone or in combination with one in the septal leaflet of the tricuspid valve. These are believed to be *endocardial-cushion defects. Defects in the muscular septum* are removed from both aortic and tricuspid valves. When three or more such defects are found, the septum may be in fact multifenestrated, and this situation is designated *"Swiss cheese"* septum.

When the repair is adjudged complete by postoperative cardiac catheterization or careful clinical study, the ventricular septum is termed *closed.* In cases where postoperative cardiac catheterization has not yet been done, but the clinical findings are suggestive although not indicative of residual shunt, the result is termed *indeterminate.* The septum is termed *open* when clinical or catheterization data indicate the presence of a shunt after operation.

After careful review of all the pertinent data and with realization that absolute accuracy is not possible, a cause was assigned for each death (Table II). Several of these causes have been commented upon previously.[7]

METHODS AND SURGICAL TECHNIQUE

Operation was advised for all patients with severe pulmonary hypertension whose pulmonary/systemic blood flow ratio was thought to be greater than 1.[2] Fifty per cent of patients in the series were from this group. Patients having ventricular septal defect without pulmonary hypertension, without evidence of cardiac enlargement or hyperemia of the lungs in the chest roentgenogram, and without electrocardiographic abnormality were not operated upon.

A Gibbon-Mayo pump-oxygenator was used in all cases. Since the fall of 1958, a modified apparatus incorporating reduced priming volume and mechanical filming of the oxygenator has been employed in operations on infants and small children. Some of the characteristics of perfusions in the early experience have been described.[7, 8] In the last 2 years, flow rates have been 2.2 L. per minute per square meter (for adults) to 2.4 L. per minute per square meter (for children), and temperature has been maintained at 37° C. by the use of a Brown-Emmons heat exchanger.[9]

Anesthetic and postoperative management have been described.[10, 11] Recent improvements include the use of halothane (Fluothane) as the anesthetic agent,[12] reliance upon systemic venous and arterial blood pressures rather than blood balance figures as guides to administration of blood, and more vigorous seeking out and treatment of metabolic acidosis in patients having low cardiac output

TABLE II. CAUSES OF HOSPITAL DEATH IN 320 CASES WITH OPERATION FOR VENTRICULAR SEPTAL DEFECT

	1955	1956	1957	1958	1959
Group 1					
Acute early pulmonary complications	6^{a}	2^{b}			
Unexpected sudden death	3^{b}	3^{b}			
Respiratory failure (apnea)		2^{b}		1^{b}	
Pseudomonas subacute bacterial endocarditis		1			
Severe hyperthermia, hypotension (? blood reaction)					1
Group 2					
Inadequate repair of mitral-valve insufficiency			1^{c}		
Inadequate repair of aortic-valve insufficiency					1
Failure in management of associated coarctation and patent ductus arteriosus					2
Failure in repair of ventricular septal defect			1^{c}	1^{c}	1^{cd}
Digitalis intoxication precipitating ventricular fibrillation					2^{d}
Sudden death sixth postoperative day during removal of ECG electrodes					1
Low cardiac output, poorly treated	1^{ce}	2^{e}	3^{e}	4^{e}	2^{ef}
Group 3					
Complete heart block		5^{cg}	5^{h}	1^{i}	
Severe early tachycardia		2		2^{b}	
Late (2 weeks) sudden tachycardia and death		1^{j}	1^{k}		
Group 4					
Chronic late pulmonary complications				2^{l}	
Low cardiac output, well treated					2^{ef}
Low cardiac output from acute right ventricular failure in operating room					1^{c}
Totals	9	17	9	10	12

a–Five had severe pulmonary hypertension. Two, including 1 with moderate pulmonary hypertension, were infants.
b–All were infants.
c–One included elsewhere also.
d–Endocardial-cushion defects.
e–All had severe pulmonary hypertension.
f–Endocardial-cushion or "Swiss cheese" defects.
g–Four had severe pulmonary hypertension; 1 had pulmonary stenosis.
h–Four were not driven immediately; 1 died in asystole in spite of pacemaker functioning since surgery.
i–Endocardial-cushion defect. Pacemaker functioning since surgery.
j–Endocardial-cushion defect. Death preceded by paroxysmal nodal tachycardia.
k–Multiple ventricular premature contractions, preoperatively and postoperatively.
l–Both infants with intractable pneumonia and atelectasis preoperatively.

after operation.[13] A median sternotomy incision has been employed since October, 1958. Since August, 1956, cardiac asystole has been used routinely, induced at first by potassium citrate and, since January, 1959, by ischemia.[14] Only a few defects were repaired through the right atrial approach.

Heart block was variously treated during this experience (Fig. 1). The method used during the past 2 years has been detailed previously.[15] Tracheostomy was employed occasionally in 1955 and early 1956, but rarely since.

A number of techniques, with and without a prosthesis, were employed in the first 3 years in an attempt to obtain complete closures of the ventricular septal defects.[16, 17] In 1958 and 1959, all high defects were repaired by direct suture with the stitches placed in a manner designed to avoid the bundle of His (Fig. 1). The line of closure is transverse to the axis of the outflow tract of the left ventricle. Interrupted sutures are placed from the posterior angle forward. Posterior to the papillary muscle of the conus, stitches are kept well away from the free edge of the septum, since it is in this area and at the posterior angle that damage to the bundle of His is most apt to occur. Along the cephalad edge of the defect the stitches actually bite firmly into the root of the aorta, just missing the aortic leaflets, which must be clearly visualized. Many defects in their anterior portion veer downward away from the aortic leaflets and here the stitches are placed only in the muscle. An assistant, by traction on the aortic clamp, brings the aortic root down against the septum as the stitches are being tied under precisely the proper tension.

Defects immediately beneath the pulmonary valve are usually somewhat triangular. Unless the defect is small, a prosthesis of Teflon is used. Endocardial-cushion defects are characteristically triangular and require the use of a prosthesis. All muscular defects have been repaired by direct suture.

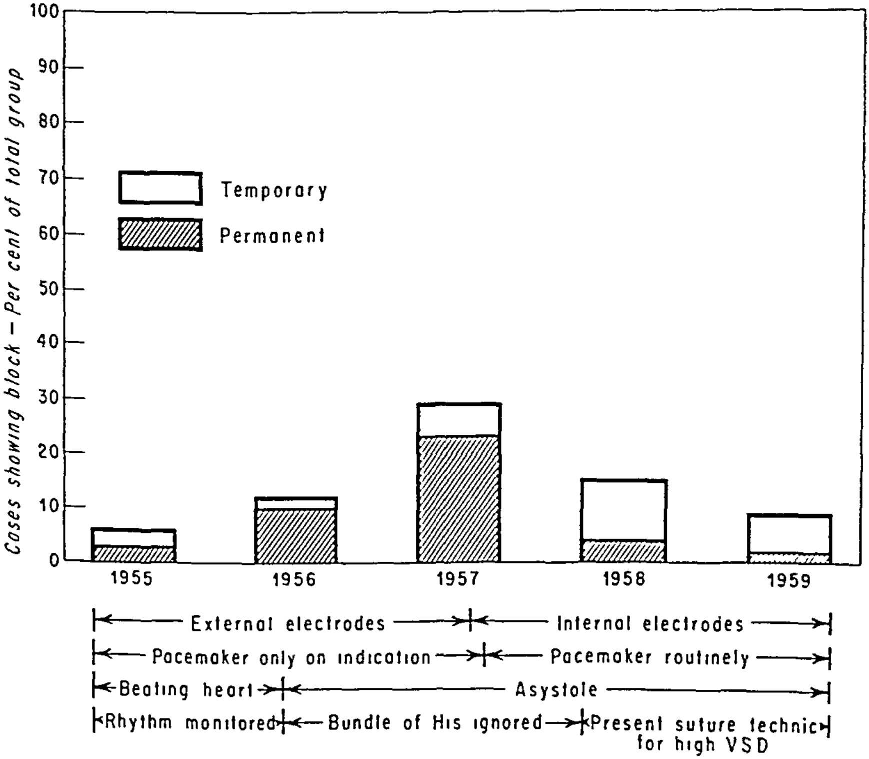

Fig 1.—Incidence of heart block and pertinent items of management following repair of ventricular septal defect

RESULTS

Hospital Mortality.—The mortality was high—43 per cent—among the 14 patients with certain additional serious cardiovascular anomalies (Table III). The combination of patent ductus arteriosus, coarctation of the aorta, and ventricular septal defect was not recognized preoperatively in 3 of the 4 patients in whom it occurred, and hence caused an especially high mortality in this group. In order to isolate the risk of surgery specifically for ventricular septal defect, the 14 patients with these particular associated anomalies have been excluded from the further observations on mortality.

TABLE III. HOSPITAL MORTALITY WITH OPERATION FOR VENTRICULAR SEPTAL DEFECT IN PATIENTS HAVING CERTAIN ASSOCIATED ANOMALIES

	1957*		1958		1959		TOTAL	
ASSOCIATED ANOMALIES	DEATHS	CASES	DEATHS	CASES	DEATHS	CASES	DEATHS	CASES
Severe mitral-valve incompetence	2	3	–	1	–	1	2	5
Severe aortic-valve incompetence	–	–	–	1	1	4	1	5
Patent ductus arteriosus and coarctation	–	1†	–	–	3	3‡	3	4

*In all tables and in the text, the period designated by a year extends from April 1 of that year to April 1 of the following year.

†Coarctation mild.

‡In 1, patent ductus arteriosus and coarctation corrected one year previously.

In the remaining group of 306 patients with ventricular septal defect (Table IV), the hospital mortality had dropped to 9 per cent in 1959. Particularly striking in that year is the rate of 6 per cent among the 18 patients 2 years of age or younger. Eight of these were infants, less than 1 year of age, in severe cardiac failure. The one death was in such an infant who at surgery was found to have an endocardial-cushion type of ventricular septal defect.

TABLE IV. HOSPITAL MORTALITY FOLLOWING REPAIR OF VENTRICULAR SEPTAL DEFECT (306 CASES), RELATED TO AGE

	1955			1956			1957			1958			1959		
	HOSP. DEATH		TOTAL CASES	HOSP. DEATH		TOTAL CASES	HOSP. DEATH		6 TOTAL CASES	HOSP. DEATH		TOTAL CASES	HOSP. DEATH		TOTAL CASES
AGE (YR.)	NO.	%		NO.	%		NO.	%		NO.	%		NO.	%	
0–2	5	63	8	8	67	12	–	0	7*	6	35	17	1	6	18
3–4	1	25	4	–	0	10	2	14	14	3	20	15	3	19	16
5–7	1	17	6	5	42	12	1	5	20	–	0	18	2	9	23
8–14	2	15	13	1	9	11	3	21	14	1	6	16	2	10	21
> 14	–	0	2	3	60	5	1	20	5	–	0	11	0	0	8
Totals	9	27	33	17	34	50	7	12	60	10	13	77	8	9	86

*No infants under 1 year of age.

Patients with mild or moderate pulmonary-artery hypertension, as well as those with pulmonary stenosis, have been operated on with a reasonable mortality throughout this experience (Table V). In the last 2 years, among the 76 patients in these categories, the only deaths occurred in 2 infants in cardiac failure operated upon in 1958. Patients with severe pulmonary-artery hypertension, as a group, had a significant hospital mortality rate, although it was reduced to 24 per cent in 1958 and 20 per cent in 1959. The pulmonary systemic blood flow ratio does appear to affect the risk of operation, since particularly in the last 2 years the risk was low where this ratio was high.

The "Swiss cheese" type of defect and endocardial-cushion defects have been associated with a higher hospital mortality than the other types (Table VI). In 1959, the risk of surgery was only 4 per cent in cases of high ventricular septal defect with severe pulmonary hypertension.

Causes of Death (Table II).—Complications considered to be the result of the perfusion technique, those in Group 1, caused most of the deaths in 1955 and 1956, but almost none thereafter. Acute early pulmonary complications disappeared by 1957. Tracheostomy was necessary occasionally in 1955 and 1956, but has been used in only 3 cases in the last 3 years. Unexpected sudden death and respiratory failure occurred in 8 patients—all infants—in 1955 and 1956. The low hospital mortality in infants in the last 2 years was achieved in large part by the near elimination of these types of deaths. The absence of renal or gross cerebral complications from the entire series is noteworthy.

The deaths tabulated in Group 2 represent inadequate surgical procedures or improper postoperative care. Group 3 includes those deaths which were due to disturbances of cardiac rhythm. In Group 4, all patients dying of low cardiac output had severe pulmonary hypertension. The patient who died in the operating room of acute right ventricular failure, manifested by falling left atrial and systemic arterial pressures and rising right atrial pressure, had identical pulmonary-artery and aortic pressures after repair of the defect as well as prior to it.

Table II again indicates that, in all years, patients who either had severe pulmonary hypertension or were of very small size were the most likely to have fatal complications. Thus, the hospital mortality in 1955 and 1956, when operative and perfusion inadequacies definitely were present, would have been lower if both infants and all patients with severe pulmonary hypertension had been denied operation.

Heart Block.—The incidence of heart block is depicted in Fig. 1, along with pertinent matters of technique. With the technique presently used, the incidence of permanent heart block was 4 per cent in 1958 and 2 per cent in 1959.

Six of the 8 patients in whom temporary or permanent heart block developed during 1955 and 1956 died in the hospital. Use of an internal electrode and routine driving of the heart with an electrical pacemaker[18] reduced the hospital mortality significantly, with 12 deaths among the 38 patients having temporary or permanent heart block in 1957, 1958, and 1959. Yet the continuing serious import of permanent heart block is indicated by the fact that although in 1957 9 patients with complete heart block left the hospital alive, 4 of them died some months later from Stokes-Adams attacks.

There were no instances of heart block after repair of a muscular defect or a defect immediately beneath the pulmonary-valve ring. Block occurred in 1 patient with a "Swiss cheese" defect, and in 3 of the 11 patients with endocardial-cushion defect.

Completeness of Repair.—Regrettably, in 1955, one third of the patients had an open ventricular septum after operation (Table VII). This resulted from inexperience in methods of exposure within the right ventricle, haste during the repair because of doubts as to the safety of perfusion, uncertainty as

Table V. Mortality Following Repair of Ventricular Septal Defect

PULMONARY-ARTERY HYPERTENSION	1955			1956			1957			1958			1959		
	HOSP. DEATH		TOTAL CASES	HOSP. DEATH		TOTAL CASES	HOSP. DEATH		TOTAL CASES	HOSP. DEATH		TOTAL CASES	HOSP. DEATH		TOTAL CASES
	NO.	%		NO.	%		NO.	%		NO.	%		NO.	%	
Mild	–	0	7	1	9	11	–	0	6	–	0	17	–	0	14
Moderate	2*	50	4	–	0	7	1	5	20	2*	10	21	–	0	20
Severe	7	33	21	14	47	30	5	17	29	8	24	33	8	20	41
High $\frac{\text{pulm.}}{\text{sysm.}}$ flow ratio	4	24	17	14	52	27	2	12	17	4	21	19	2	10	21
Moderate $\frac{\text{pulm.}}{\text{sysm.}}$ flow ratio	2	100	2	–	0	2	3	25	12	3	23	13	4	25	16
Low $\frac{\text{pulm.}}{\text{sysm.}}$ flow ratio	1	50	2	–	0	1	–	0	–	1	100	1	2	50	4
Mild, with pulmonary stenosis	–	0	1	2	100	2	1	20	5	–	0	6	–	0	11
Totals	9	27	33	17	34	50	7	12	60	10	13	77	8	9	86

*Both were infants.

TABLE VI. MORTALITY IN VENTRICULAR SEPTAL DEFECT ACCORDING TO ANATOMIC TYPE OF VENTRICULAR SEPTAL DEFECT

PULMONARY HYPERTENSION	TYPE OF DEFECT	1955			1956			1957			1958			1959		
		HOSP. DEATH		TOTAL CASES	HOSP. DEATH		TOTAL CASES	HOSP. DEATH		TOTAL CASES	HOSP. DEATH		TOTAL CASES	HOSP. DEATH		TOTAL CASES
		NO.	%		NO.	%		NO.	%		NO.	%		NO.	%	
Mild	High	-	0	7	1	11	9	-	0	6	-	0	16	-	0	13
	Beneath pulm. valve	-	-	-	-	-	-	-	-	-	-	-	-	-	0	1
	Muscular	-	-	-	-	0	1	-	-	-	-	0	1	-	-	-
	"Swiss cheese"	-	-	-	-	0	1	-	-	-	-	-	-	-	-	-
	Endocardial cushion	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Moderate	High	2*	50	4	-	0	7	1	6	17	2*	12	17	-	0	18
	Beneath pulm. valve	-	-	-	-	-	-	-	-	-	-	0	1	-	0	2
	Muscular	-	-	-	-	-	-	-	0	2	-	0	3	-	-	-
	"Swiss cheese"	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	Endocardial cushion	-	-	-	-	-	-	-	0	1	-	-	-	-	-	-
Severe	High	5	28	18	9	39	23	3	13	24	6	23	26	1	4	27
	Beneath pulm. valve	1	50	2	1	100	1	1	100	1	-	0	2	1	33	3
	Muscular	-	-	-	1	100	1	-	0	1	-	0	3	-	0	3
	"Swiss cheese"	1	100	1	1	33	3	1	33	3	-	-	-	2	100	2
	Endocardial cushion	-	-	-	2	100	2	-	-	-	2	100	2	4	67	6
Pulmonary stenosis	High	-	0	1	2	100	2	1	20	5	-	0	5	-	0	10
	Muscular	-	-	-	-	-	-	-	-	-	-	0	1	-	0	1
Totals		9	27	33	17	34	50	7	12	60	10	13	77	8	9	86

*Infants

TABLE VII. STATUS OF VENTRICULAR SEPTUM AFTER OPERATION FOR VENTRICULAR SEPTAL DEFECT

TYPE OF VENTRICULAR SEPTAL DEFECT	1955					1956					1957					1958					1959				
	OPEN		INDETERMINATE		TOTAL CASES	OPEN		INDETERMINATE		TOTAL CASES	OPEN		INDETERMINATE		TOTAL CASES	OPEN		INDETERMINATE		TOTAL CASES	OPEN		INDETERMINATE		TOTAL CASES
	NO.	%	NO.	%		NO.	%	NO.	%		NO.	%	NO.	%		NO.	%	NO.	%		NO.	%	NO.	%	
High	9	32	3	6	30	6*	16	1	2	41	2†	4	2	4	55	7	11	2	3	66	2†	3	4	5	76
Beneath pulm. valve	2	100	-	-	2	1‡	100	-	-	1	-	-	-	-	1	-	-	-	-	3	-	-	-	-	5
Muscular	-	-	-	-	0	1	50	-	-	2	-	-	-	-	4	-	-	-	-	8	-	-	-	-	5
"Swiss cheese"	-	-	-	-	1	2†	50	-	-	4	1§	33	-	-	3	-	-	-	-	0	1§	50	-	-	2
Endocardial cushion	-	-	-	-	0	-	-	-	-	2	-	-	-	-	1	1	50	-	-	2	1	17	1	17	6
Totals	11	33	3	9	33	10	20	1	2	50	3	5	2	3	64	8	10	2	3	79	4	4	5	5	94

*Only small L→R shunt in 3 of these 6.

†Only small L→R shunt in 1 of these 2.

‡Following subacute bacterial endocarditis.

§Only small L→R shunt in 1.

to exact pathologic anatomy in many instances, and lack of knowledge concerning proper techniques for closure of the defect. When insertion of a stitch produced atrioventricular dissociation, it was removed. Reluctance to replace it in that position frequently resulted in incompleteness of repair.

The adoption of induced asystole in August, 1956, provided better exposure within the heart. Confidence as to the safety of perfusion allowed more deliberate intracardiac surgery. The technique of repair was directed solely toward obtaining complete closure of the defect. Since knowledge of the cause of heart block was incomplete at that time, no attempt was made to avoid the region occupied by the bundle of His. Consequently, the incidence of open septum among patients operated upon in 1957 was reduced to 5 per cent, but the incidence of permanent heart block rose sharply to 23 per cent.

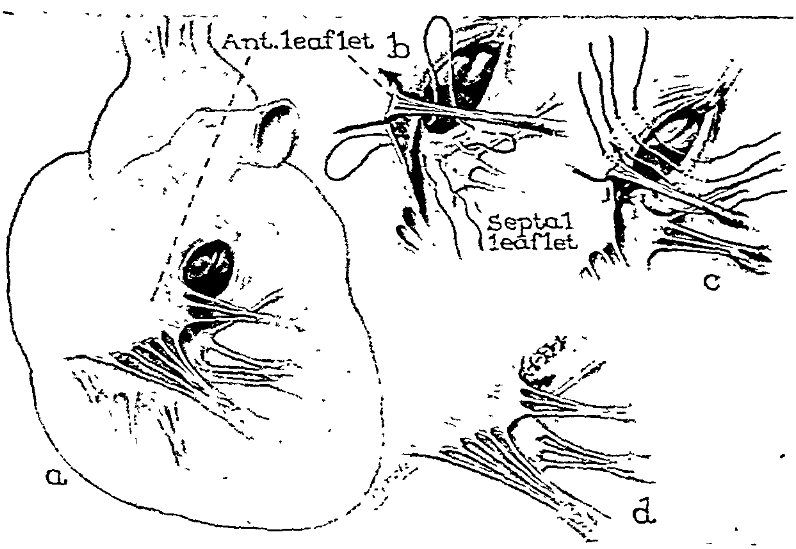

Fig. 2.—Technique of repair of high ventricular septal defect. *a*, Anatomic situation. *b*, A small retractor elevates the anterior corner of the defect. The first stitch is placed posteriorly in the manner shown, with care to avoid the free edge of the septum posterior to the papillary muscle of the conus. *c*, After all stitches are placed, the posterior one is tied, the knot lying on the right atrial aspect of the base of the tricuspid leaflets. *d*, No interference with tricuspid function is produced. No chordae tendineae are severed and no incision is made in the tricuspid leaflets.

This necessitated the change to the technique of repair used in 1958 and 1959 (Fig. 2). Probably because stitches near the posterior angle of the high ventricular septal defects were improperly located or too shallow, the incidence of open septum after operation rose to 10 per cent in 1958. In 1959, the incidence of known incomplete repair was reduced to 4 per cent. Since in this experience the presence of an open septum has always become manifest soon after operation, it is not feared that a longer follow-up will appreciably alter this figure.

The "Swiss cheese" type of defect, by its nature, continues to be sometimes difficult of total repair. Proper understanding of the anatomy and methods of exposure and repair of the endocardial-cushion type of ventricular septal defect have only recently been acquired.

COMMENT

Good results at a low hospital mortality have been obtained throughout this experience in children and adults having mild or moderate pulmonary hypertension. A similar experience is reported by others.[19, 20] Improved knowledge and techniques, gained through the investigations and experiences of others and ourselves, were required to achieve good results in infants and in patients with severe pulmonary hypertension.

The avoidance of deleterious effects from perfusion is probably more difficult in infants than in large patients. High flow rates were employed in the last 2 years, and use of substances such as antifoam was eliminated. The possibility of gaseous emboli was minimized by careful control of the temperature of blood before and during perfusion and by an alteration of the intracardiac sucker system. Use of a mechanical filmer for the oxygenator eliminated the hemodilution associated with the previously used saline filming technique. Maintenance of anesthesia by Fluothane, rather than by intravenously administered agents supplemented by relaxants, assured rapid recovery of the infant from the effects of anesthesia.

Good results in patients with severe pulmonary hypertension require a precise surgical technique and careful management after operation. The closure of high defects by direct suture, as practiced in the last 2 years, has resulted in a high incidence of complete repairs and a low incidence of heart block. Induced asystole provides excellent exposure, and has not seemed to add significantly to the risk of the operation. In the last few years, patients in this category usually have had an uncomplicated course. Occasionally there is evidence of low cardiac output early after perfusion, and failure to treat it vigorously resulted in some deaths. Maintenance of proper blood volume, prompt action against the metabolic acidosis which usually becomes marked under these circumstances, and digitalization, when required, have virtually eliminated this as a cause of death in our recent experience.

SUMMARY

An analysis is presented of 320 consecutive cases of ventricular septal defect in which operation was performed at the Mayo Clinic. A low hospital mortality and good results were achieved throughout the 5-year experience in older patients with mild or moderate pulmonary hypertension. Early, the mortality was high among infants and among all patients with severe pulmonary hypertension. Refinements in techniques of perfusion, operation, and management produced markedly improved results in these groups.

REFERENCES

1. Kirklin, J. W., Ellis, F. H., Jr., McGoon, D. C., DuShane, J. W., and Swan, H. J. C.: Surgical Treatment for the Tetralogy of Fallot by Open Intracardiac Repair, J. Thoracic Surg. 37: 22-46, 1959.
2. DuShane, J. W., and Kirklin, J. W.: Selection for Surgery of Patients With Ventricular Septal Defect and Pulmonary Hypertension, Circulation 21: 13-20, 1960.

3. DuShane, J. W., Weidman, W. H., Brandenburg, R. O., and Kirklin, J. W.: The Electrocardiogram in Children With Ventricular Septal Defect and Severe Pulmonary Hypertension: Correlation With Response of Pulmonary Arterial Pressure to Surgical Repair, Circulation 21: 49-54, 1960.
4. Vickers, C. W., Kincaid, O. W., DuShane, J. W., and Kirklin, J. W.: Ventricular Septal Defect and Severe Pulmonary Hypertension: Radiologic Considerations in Selection of Patients for Surgery, Radiology 75: 69-79, 1960.
5. Ziegler, R. F.: Electrocardiographic Studies in Normal Infants and Children, Springfield, Ill., 1951, Charles C Thomas, publisher, 207 pp.
6. Cayler, G. G., Ongley, P., and Nadas, A. S.: Relation of Systolic Pressure in the Right Ventricle to the Electrocardiogram: A Study of Patients With Pulmonary Stenosis and Intact Ventricular Septum, New England J. Med. 258: 979-982, 1958.
7. Kirklin, J. W., McGoon, D. C., Patrick, R. T., and Theye, R. A.: What Is Adequate Perfusion? *in* U. S. National Institutes of Health, Surgery Study Section: Extracorporeal Circulation, Springfield, Ill., 1958, Charles C Thomas, publisher, pp. 125-138.
8. Moffitt, E. A., Patrick, R. T., Swan, H. J. C., and Donald, D. E.: A Study of Blood Flow, Venous Blood Oxygen Saturation, Blood Pressure, and Peripheral Resistance During Total Body Perfusion, Anesthesiology 20: 18-26, 1959.
9. Brown, I. W., Jr., Smith, W. W., and Emmons, W. O.: An Efficient Blood Heat Exchanger for Use With Extracorporeal Circulation, Surgery 44: 372-377, 1958.
10. Moffitt, E. A., and Theye, R. A.: Management of Anaesthesia, Perfusion and Supportive Care During Open Intracardiac Operations and Extracorporeal Circulation, Brit. J. Anaesth. 31: 411-416, 1959.
11. Lyons, W. S., DuShane, J. W., and Kirklin, J. W.: Postoperative Care After Whole-Body Perfusion and Open Intracardiac Operations, J. A. M. A. 173: 625-630, 1960.
12. Dawson, B., Theye, R. A., and Kirklin, J. W.: Halothane in Open Cardiac Operations: A Technic for Use With Extracorporeal Circulation, Anesth. & Analg. 39: 59-63, 1960.
13. Ito, I., Faulkner, W. R., and Kolff, W. J.: Metabolic Acidosis and Its Correction in Patients Undergoing Open-Heart Operation, Cleveland Clin. Quart. 24: 193-203, 1957.
14. Crafoord, C., Norberg, B., and Senning, Å.: Clinical Studies in Extracorporeal Circulation With a Heart-Lung Machine, Acta chir. scandinav. 112: 220-245, 1957.
15. Lauer, R. M., Ongley, P. A., DuShane, J. W., and Kirklin, J. W.: Heart Block Occurring After Repair of Ventricular Septal Defect in Children, Circulation (In press).
16. Kirklin, J. W., Harshbarger, H. G., Donald, D. E., and Edwards, J. E.: Surgical Correction of Ventricular Septal Defect: Anatomic and Technical Considerations, J. THORACIC SURG. 33: 45-57, 1957.
17. Kirklin, J. W., and McGoon, D. C.: Surgical Technique for Repair of High Ventricular Septal Defects, J. THORACIC SURG. 35: 584-590, 1958.
18. Weirich, W. L., Gott, V. L., and Lillehei, C. W.: The Treatment of Complete Heart Block by the Combined Use of a Myocardial Electrode and an Artificial Pacemaker, Am. Coll. Surgeons, Clin Cong. (43rd), Proc. S. Forum 8: 360-363, 1958.
19. Cooley, D. A.: Current Status of Surgical Treatment of Ventricular Septal Defect, Dis. Chest 35: 651-662, 1959.
20. Kay, E. B., Sambhi, M. P., Nogueira, C., and Zimmerman, H. A.: Treatment of Ventricular Septal Defects, J. A. M. A. 165: 2168-2174, 1957.

(For Discussion, see page 799.)

THE CLOSURE OF ATRIAL SEPTAL DEFECTS UTILIZING GENERAL HYPOTHERMIA

The Effectiveness of Treatment as Determined by Cardiac Catheterization

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In 1954 a number of surgical methods for the correction of atrial septal defect were in use at various centers in this country and in Europe. Among the most popular of these were atrioseptopexy,[1, 2] various other methods of external suture,[3, 4] and the circumclusion operation devised by Sondergaard.[5] The atrial well, introduced by Gross,[6] was found to permit a direct approach to these lesions and this technique was adopted with considerable success by Kirklin and his associates.[7, 8] At about this same time, Lewis[9] and Swan[10] demonstrated the safety and practicability of general hypothermia and showed that the extended period of circulatory occlusion made possible by hypothermia provided opportunity for the suture of atrial septal defects under direct vision. The open operation with hypothermia appeared to have distinct advantages over the various closed or semi-open techniques and this method was selected for use at the National Heart Institute. Between 1954 and 1957, 36 patients with interatrial communications were operated upon with general hypothermia. In 34 patients, in whom repair was carried out, opportunity was afforded for an assessment of the effectiveness of the closure by postoperative cardiac catheterization or autopsy examination. The results of these studies, a description of the techniques employed, and a discussion of the factors limiting the effectiveness of the method are presented.

CLINICAL MATERIAL AND DIAGNOSTIC METHODS

The 36 patients ranged in age from 6 to 49 years; only 11 of them were 15 years or less. With one exception, each presented the characteristic physical, radiographic, and electrocardiographic findings of atrial septal defect. In the 1 patient, subsequently shown to have incomplete atrioventricular canal, the electrocardiogram revealed left axis deviation. Cardiac catheterization was performed in every patient and in each a left-to-right shunt entering the right

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atrium was demonstrated. At the National Heart Institute, the presence, location, and magnitude of left-to-right shunts are determined by the results of indicator-dilution curves and inert foreign gas tests. In the latter method the patient inhales nitrous oxide (N_2O) or radioactive krypton (Kr^{85}) for 30 seconds as blood samples are drawn simultaneously from the right heart or pulmonary artery and a peripheral artery. The presence and magnitude of any left-to-right shunt are indicated by the relative amounts of inert gas present in the two samples.[11, 12] The N_2O test has been proved to be distinctly superior to the method of measuring oxygen differences in several hundred patients studied by both techniques. It not only provides a more sensitive method for detecting a shunt but furnishes a reliable estimate of its magnitude in terms of the ratio of pulmonary to systemic blood flow.[13] A summary of the data obtained at right heart catheterization is presented in Table I.

Significant pulmonary hypertension, that is, a mean pulmonary arterial pressure greater than 22 mm. Hg, was present in 13 patients. In 2 of them (C. R. and T. S.) the pulmonary and systemic pressures were equal and the shunt across the atrial defect was bidirectional. The presence of a sinus venosus type of defect with partial anomalous pulmonary venous drainage was established in 2 patients by the catheter position; indicator-dilution curves were not routinely employed to characterize the drainage pathways of the pulmonary veins at that time.

OPERATIVE TECHNIQUE AND FINDINGS

Every patient was digitalized before operation because of the experimental demonstration that myocardial failure occurring with circulatory occlusion during hypothermia could be prevented by digitalis.[14] For each patient, 500 c.c. of freshly drawn heparinized blood was oxygenated by bubbling oxygen through it and used for gravity perfusion of the coronary arteries during the period of cardiotomy.[15, 16] After the induction of anesthesia with pentobarbital, succinylcholine, and nitrous oxide, the patients were cooled by immersion to an esophageal temperature of 32° to 33° C. The temperature drifted to an ultimate level of 29° to 30° C. at the time of inflow occlusion. Mechanical ventilation with 65 per cent oxygen and 35 per cent nitrous oxide was provided. A right thoracotomy was employed early in the series but median sternotomy was utilized in the majority of patients. After the venae cavae had been encircled with tapes, the ascending aorta was freed to permit subsequent occlusion (Fig. 1). The size and position of the defect, the entrances of the pulmonary veins and the competency of the mitral and tricuspid valves were assessed by palpation through the right atrial appendage (Fig. 2). A partially occluding clamp was applied to the wall of the atrium and a generous incision made within the excluded segment (Fig. 3). The venae cavae were then occluded and after the heart was allowed to empty, the aorta was cross-clamped below the origin of the innominate artery. The coronary perfusion needle (Fig. 3) was inserted into the aorta and oxygenated blood perfused by gravity from a reservoir elevated

TABLE I. HEMODYNAMIC AND OPERATIVE FINDINGS

PATIENT	AGE	PREOP. CATHETERIZATION			TYPE AND SIZE OF DEFECT	POSTOP. CATHETERIZATION			COMMENT
		PA PRESSURE (MM./HG)		$N_2O\%$ AND LOCATION		PA PRESSURE (MM./HG)		$N_2O\%$ AND LOCATION	
		S/D	MEAN			S/D	MEAN		
M. L.	36	35/10	21	50 RA†	Secundum, 5 cm.	35/15	25	7 RA	
L. W	24	48/18	32	70 RA†	Secundum, 6 cm.	31/7	17	53 RA	
L. H.	24	30/8	18	—	Secundum, 2 cm.	—	—	—	Died 10th day; autopsy closed
C. R.	35	120/48	74	36 RA	Secundum, 3 cm.	—	—	—	Died 12 hours; autopsy closed
D. McD.	46	40/16	26	85 RA	Secundum, 3 cm.	30/12	19	46 PA	
D. S.	34	80/42	44	83 RA	Sinus venosus	70/28	44	49 PA	
M. K.	22	30/9	16	89 RA	Secundum (fenestrated), 4 cm.	16/6	12	4 PA	
D. B.	41	34/10	21	39 RA	Secundum, 3 cm.	—	—	11 RA	
C. N.	43	74/28	45	43 RA	Secundum, 4 cm.	25/2*	—	29 RA	
E. Del M.	47	85/36	58	48 PA	Secundum, 5 cm.	52/20	38	10 RA	
J. K.	15	23/7	13	67 PA	Secundum, 5 cm.	28/15	18	12 PA	
C. R.	23	28/10	14	66 RA	Secundum, 4 cm.	13/4	7	12 RA	
B. W.	39	32/10	21	48 RA	Secundum, 5 cm.	22/5	9	8 PA	
K. C.	39	42/17	22	72 RA	Secundum, 6 cm.	23/9	15	13 PA	
B. C.	49	34/8	21	32 RA	Secundum, 4 cm.	—	—	—	Died 1 year; no follow-up
B. Q.	18	30/9	16	56 RA	Secundum, 7 cm.	16/5	10	8 PA	
I. T.	37	82/10*	—	48 RA	Secundum, 6 cm.	90/10*	—	42 RV	
C. M.	27	25/11	20	82 RA	Secundum, 6 cm.	22/7	12	40 PA	Reoperated; extracorporeal circulation
J. T.	18	40/15	24	52 RA	Secundum, 7 cm.	—	—	—	No attempt made to repair defect
B. S.	10	35/10*	—	62 RV	Secundum, 5 cm.	18/8	12	8 PA	
D. E.	7	22/5	12	63 RA	Sinus venosus	15/7	10	30 PA	
E. H.	6	35/9	23	56 RA	Secundum, 3 cm.	29/5*	—	13 RA	
M. M.	27	37/7*	—	61 RV	Atrioventricular canal	—	—	—	Died at operation
W. H.	18	25/6	17	71 RA	Sinus venosus	22/8	14	36 PA	
R. J.	9	15/4	7	44 RA	Secundum, 3 cm.	26/9	15	23 PA	
B. S.	14	25/8	16	62 PA	Secundum, 3 cm.	19/8	12	7 PA	
S. H.	14	24/7	12	57 RV	Secundum, 2 cm.	23/10	14	12 PA	
C. O.	10	18/6	12	50 PA	Secundum, 4 cm.	22/7	12	12 PA	
L. B.	27	22/10	12	54 PA	Secundum (fenestrated), 5 cm.	18/6	9	11 PA	
M. E.	32	35/10	16	70 PA	Secundum, 3 cm.	25/10	13	12 PA	
M. K.	9	26/10	16	59 PA	Sinus venosus	16/2	6	8 RA	
R. R.	9	28/15	21	37 PA	Secundum, 3 cm.	32/15	23	6 PA	
L. W.	47	34/15	19	60 PA	Secundum (fenestrated), 7 cm.	25/6	14	8 PA	
G. R.	37	24/14	16	32 PA	Secundum, 3 cm.	18/7	12	5 PA	
D. S.	12	125/70	95	38 PA	Secundum, 2 cm. Reverse ductus	120/45	70	0 RA 10 PA	Died following closure reverse ductus
C. A.	31	20/7	12	51 PA	Secundum, 3 cm.	27/13	18	[illegible]	

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*Right

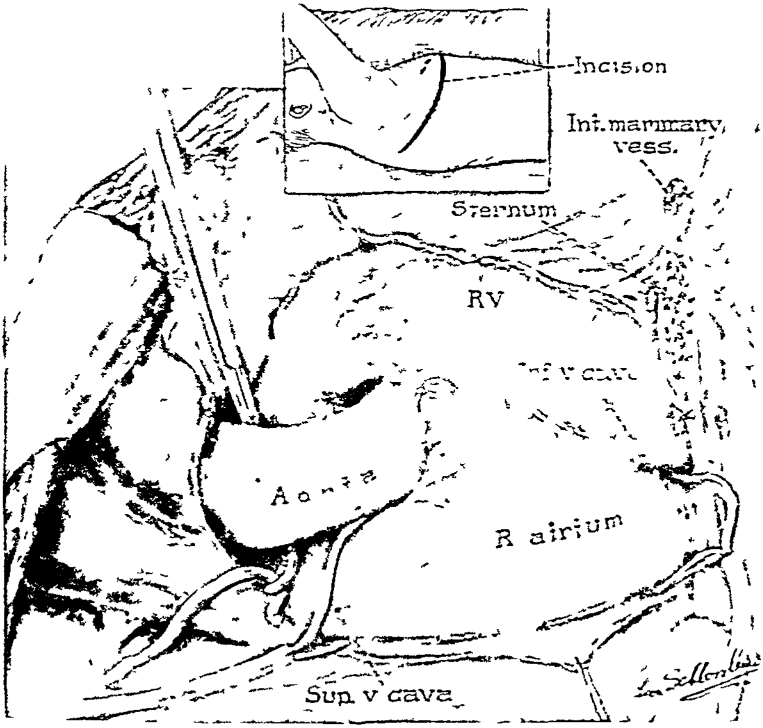
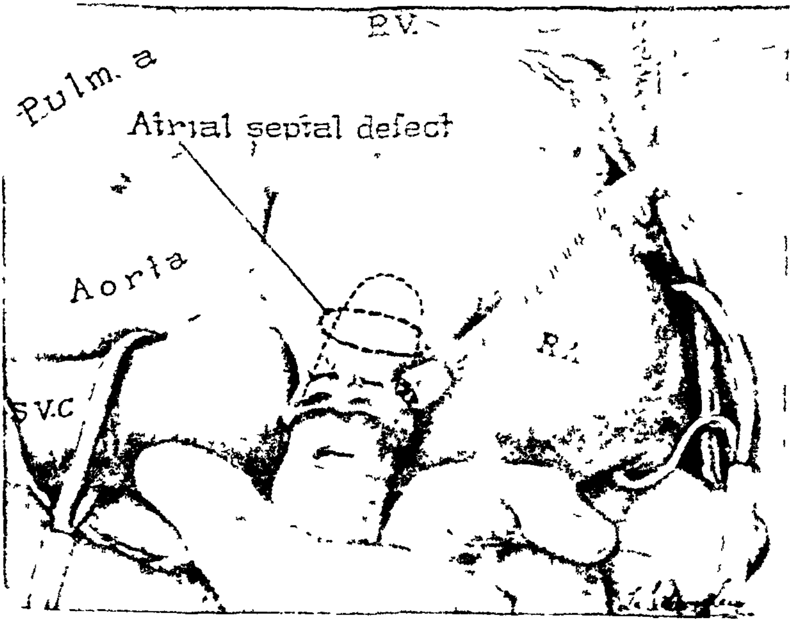


Fig 1—Surgical exposure employed in the direct closure of atrial septal defects with general hypothermia A median sternotomy rather than a transverse thoracotomy was most often employed



F[illegible] —The location and size of the defect and the consistency of its margins are assessed by digital examination before circulatory occlusion

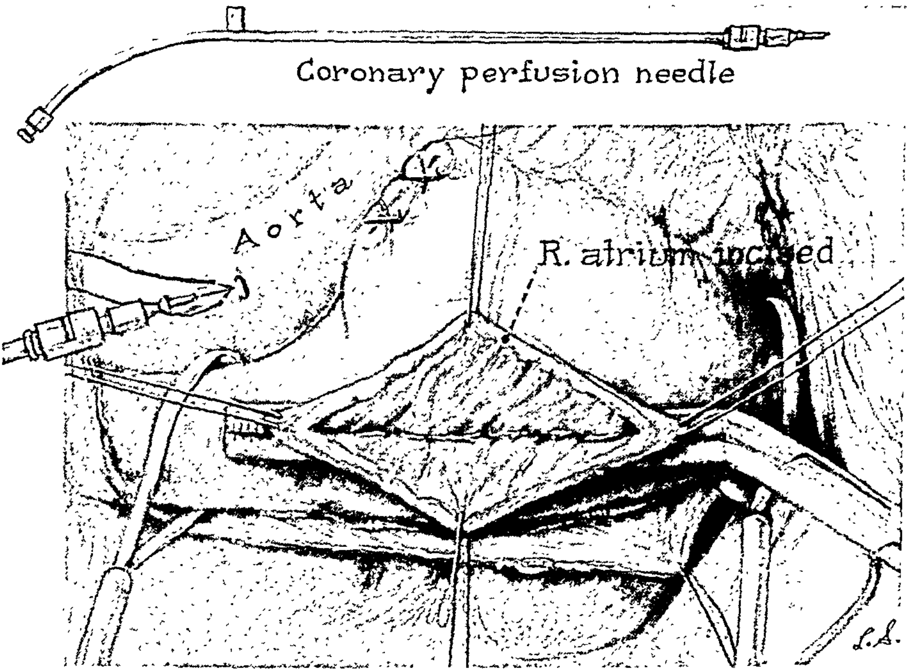


Fig. 3.—The right atriotomy is made over a partially occluding clamp. The coronary perfusion needle (designed by Dr. James Jude) will be inserted through the mattress suture in the wall of the aorta.

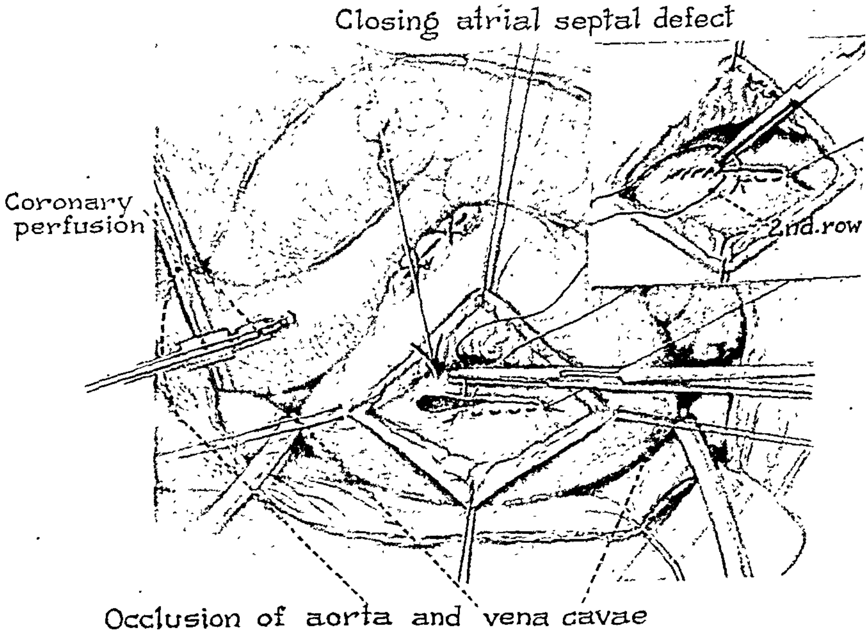

Closing atrial septal defect
Coronary perfusion
2nd. row
Occlusion of aorta and vena cavae

Fig. 4.—The defect is closed by two layers of sutures as shown

100 cm. above the table. In the first 9 patients, the defect was closed with a single continuous suture, but, in all subsequent ones, two layers of sutures were placed. The first was a continuous everting mattress suture which was drawn up after it had been placed and as the left atrium was flooded with blood from the inferior vena cava. The everted margins of the defect were then approximated by a second over and over row (Fig 4). The right atrium and ventricle were then filled with blood, the clamp reapplied to the atriotomy and venous return restored. The periods of circulatory occlusion ranged from 3 to 9 minutes and averaged 5.5 minutes

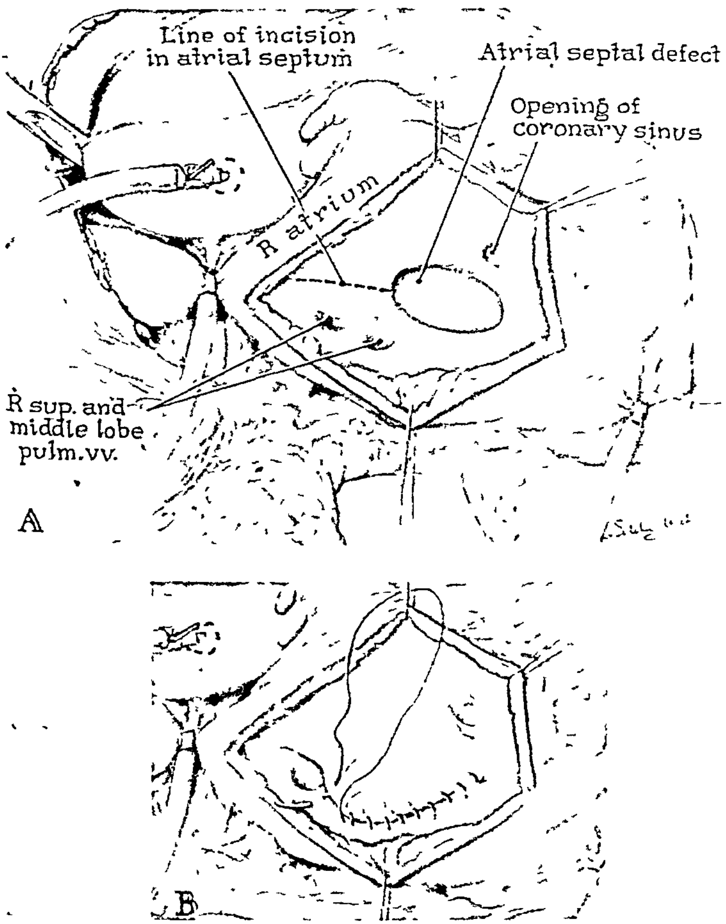

Line of incision in atrial septum
Atrial septal defect
Opening of coronary sinus
R atrium
R sup. and middle lobe pulm.vv.
A
B

Fig 5—The method employed for the correction of the sinus venosus type of defect by direct suture (From Bahnson, Spencer, and Neill J Thoracic Surg 36 777, 1958)

In 2 of the 4 patients with sinus venosus defects and anomalous drainage of the upper and middle lobe pulmonary veins, an attempt at complete correction was made by the method described by Bahnson[17] (Fig 5) In the others, the atrial defect was closed and the pulmonary arteries supplying the upper and middle lobes were ligated A description of the lesion encountered in the remaining patients is included in Table I

RESULTS

Three patients died after operation. In 1 (M. M.) the unsuccessful attempt at correction of incomplete atrioventricular canal was followed by irreversible ventricular fibrillation. Patient C. R., with pulmonary hypertension and bidirectional shunt, died after 12 hours, and L. H. died suddenly on the tenth postoperative day after the onset of an acute arrhythmia. In each of these 2 patients, complete closure of the defects was demonstrated at autopsy. A fourth patient (B. C.) died at home 1 year after operation; no postoperative catheterization had been performed. In 1 patient (J. T.), a defect, estimated by palpation to be more than 7 cm. in diameter, was present and closure was not attempted.

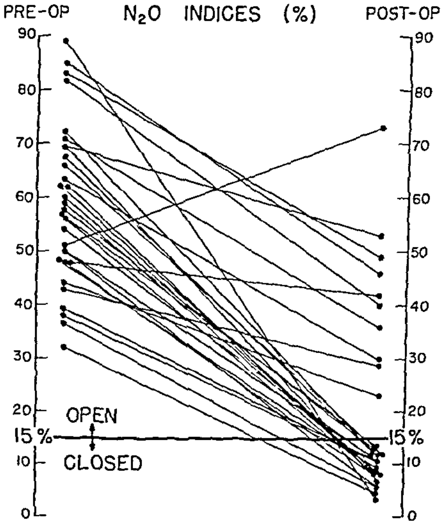


Fig. 6.—Nitrous oxide indices recorded at cardiac catheterization before (left) and after (right) operation in 31 patients with septum secundum or sinus venosus defects. A nitrous oxide index of 15 per cent or greater indicates the presence of a left-to-right shunt. Indices of 40 and 60 per cent indicate pulmonary to systemic flow ratios of 1.5 and 2.5, respectively.

Postoperative cardiac catheterizations were carried out in the 31 surviving patients with sinus venosus or septum secundum defects in whom correction had been attempted. The results of these studies are presented in detail in Table I and shown graphically in Fig. 6. The N_2O indices were clearly indicative of a residual left-to-right shunt in 10 patients. In 7 of these patients, the shunts were of relatively large magnitude and the pulmonary to systemic flow ratios were 1.4:1 or greater. *In each patient in whom the results of N_2O tests indicated a residual shunt*, arterial indicator-dilution curves recorded after right heart injection were also abnormal and confirmed the presence of a persistent communication.

COMMENT

Atrial septal defects of the usual or secundum variety are anatomically distinct from those of the sinus venosus type and the results of operative treatment must be considered accordingly. In each of the patients with septum secundum defects, regardless of size, closure was of necessity carried out by direct suture and it was considered likely that the frequency of incomplete repair would be higher among patients with defects of large size. In Fig. 7 the incidence of complete repair is plotted in relation to the size of the defect encountered at operation. It can be seen that there is no absolute correlation between the size of the defect and the incidence of incomplete closure. It was of interest, however, that of the seven largest defects (6 cm or greater in diameter) four were open and of the thirteen smallest ones (3 cm. or less in diameter) only three were incompletely repaired. In Fig. 8 the operative result is similarly indicated but the patients are arranged in the chronological order in which the operations were carried out. It is apparent that complete closure was achieved with greater frequency late in the series, reflecting increased familiarity with the operation and more deliberate attention to the repair. It should be pointed out, however, that among the first 16 patients only 1 was a child, aged 15 years

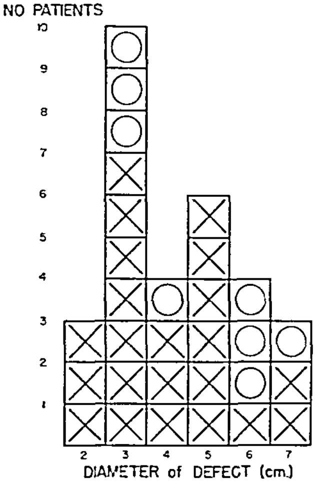


Fig 7.—Effectiveness of the repair of septum secundum defects in relation to their size. Complete closure is indicated by a *cross*, a residual communication by a *circle*.

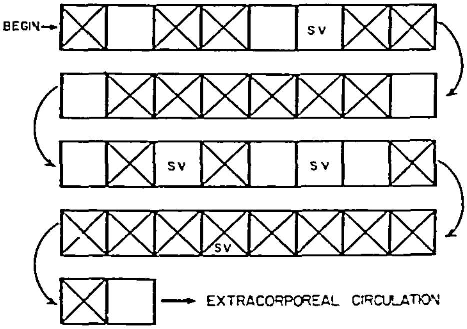


Fig 8.—Effectiveness of repair in relation to the chronologic order in which the patients were operated upon. The initials *S V* indicate sinus venosus defects.

or less, while among the last 18 patients 10 were in this age group. When age alone was considered in relation to the effectiveness of the operative treatment of secundum defects it was found that among the 9 children only 1 had a residual shunt while in the 21 adults a residual shunt was present in 7. There was no correlation between the adequacy of repair and the duration of circulatory occlusion.

In 2 patients with sinus venosus defects (D. S. and D. E.) only the interatrial communication was closed and the segmental pulmonary arteries supplying the upper and middle lobes were ligated. In each, the magnitude of the left-to-right shunt was reduced, but the residual shunt, presumably from the anomalous veins, was surprisingly large. In 2 additional patients (W. N. and M. K.), complete correction of the malformation by direct suture was attempted (Fig. 5) and was successful in 1 of them. A disadvantage of direct suture in the correction of sinus venosus defects is danger of constriction of the superior vena cava and subsequent thrombosis of it or one of the pulmonary veins. This complication was not observed, however, in either patient.

No detailed correlation was made between the clinical and hemodynamic findings at the time of postoperative study. In general, however, the presistence of fixed splitting of the pulmonary second sound was indicative of a large residual shunt. In some patients, however (for example, R. J.), normal closure of the second sound during expiration was noted postoperatively and, on the basis of the physical findings alone, the defect would have been considered completely closed.

In the latter part of the operative series, arterial indicator-dilution curves were recorded, after injection into the right superior pulmonary vein, before the thoracotomy was closed. Curves of normal contour were obtained at operation in 2 patients (C. M. and R. J.) who were later shown at catheterization to have residual shunts. It seems probable, therefore, that complete closure was initially achieved in these patients but that the suture line dehisced in the postoperative period. This view is substantiated by the findings in 2 patients with residual shunts of large magnitude who have been operated upon again with the aid of extracorporeal circulation. In each, a series of holes of varying size was present in the initial suture line. It was apparent that many sutures had torn through the septum and the initial single defect had only been converted into many smaller ones.

The primary cause for incomplete correction among the patients described is considered to be the relatively brief period of cardiotomy provided by general hypothermia. It was often difficult to define precisely the margins of the defect and direct suture was always necessary, even when it resulted in a closure under tension. In many patients there was obvious need for prosthetic replacement of a portion of the septum but the insertion of such material was patently impossible in the time allowed. Although repetitive periods of occlusion have been employed by Kirby[15] and others to extend the total period of cardiotomy, even this technique would not seem adequate for the time-consuming reconstruction often necessary. For these reasons, the use of general hypothermia in the treatment of patients with atrial septal defect has been abandoned and the correction of this malformation is always undertaken during the prolonged period of circulatory exclusion made possible by extracorporeal circulation. The advantages of the latter method seem apparent at this time but proof of its value will, of course, depend upon a detailed hemodynamic evaluation such as that presented above.

SUMMARY

In 34 patients with atrial septal defects of the septum secundum or sinus venosus type, correction was attempted by direct suture during a period of circulatory occlusion provided by general hypothermia. The effectiveness of the repair was assessed in 33 by postoperative cardiac catheterization or autopsy examination. A residual left-to-right shunt was present in 7 of 29 patients with secundum defects and in 3 of 4 patients with sinus venosus defects. These poor results were attributed to the brief period of cardiotomy provided by hypothermia which necessitated closure by direct suture in every instance. Since extracorporeal circulation permits a prolonged intracardiac procedure and the insertion of a prosthesis if necessary, this technique is now considered preferable in the treatment of all patients with atrial septal defect

REFERENCES

1. Bailey, C. P., Downing, D. F., Geckeler, G. D., Litkoff, W., Goldberg, H., Scott, J. C., Janton, O., and Redondo Ramirez, H. P.: Congenital Interatrial Communications: Clinical and Surgical Considerations With a Description of a New Surgical Technic: Atrio Septo Pexy, Ann. Intern. Med. 37: 888, 1952.
2. Bailey, C. P., Bolton, H. E., Jamison, W. L., and Neptune, W. B.: Atrio Septo-Pexy for Interatrial Septal Defects, J. THORACIC SURG. 26: 184, 1953.
3. Watkins, E., Jr., and Gross, R. E.: *Experiences With Surgical Repair of Atrial Septal Defects*, J. THORACIC SURG. 30: 469, 1955.
4. Bahnson, H. T.: Accomplishments and Possibilities in Cardiovascular Surgery, Am. J. Roentgenol. 76: 730, 1956.
5. Sondergaard, T.: Closure of Atrial Septal Defects. Report of Three Cases, Acta chir Scandinav. 107: 492, 1954.
6 Gross, R. E., Watkins, E., Pomeranz, A. A., and Goldsmith, E. I.: A Method for Surgical Closure of Interauricular Septal Defects, Surg. Gynec. & Obst. 96: 1, 1953.
7. Kirklin, J. E., Swan, H. J. C., Wood, E. H., Burchell, H. B., and Edwards, J. E.: Anatomic, Physiologic, and Surgical Considerations in Repair of Interatrial Communications in Man, J. THORACIC SURG. 29: 37, 1955.
8 McGoon, D. C., Swan, H. J. C., Brandenburg, R. O., Connolly, D. C., and Kirklin, J. W.: *Atrial Septal Defect: Factors Affecting the Surgical Mortality Rate, Circulation* 19: 195, 1959.
9. Lewis, F. J., and Taufic, M.: Closure of Atrial Septal Defects With the Aid of Hypothermia; Experimental Accomplishments and the Report of One Successful Case, Surgery 33: 52, 1953.
10. Swan, H.: Surgical Closure of Interauricular Septal Defects, J. A. M. A. 151: 792, 1953.
11 Morrow, A. G., Sanders, R. J., and Braunwald, E.: The Nitrous Oxide Test: An Improved Method for the Detection of Left to Right Shunts, Circulation 17: 281, 1958.
12 Sanders, R. J., and Morrow, A. G.: The Diagnosis of Circulatory Shunts by the Nitrous Oxide Test. Improvements in Technic and Methods for Quantification of the Shunt, Circulation 18: 856, 1958.
13. Sanders, R. J., Cooper, T., and Morrow, A. G.: An Evaluation of the Nitrous Oxide Method for the *Quantification of Left to Right Shunts: An Experimental Comparison* of the Gasometric Technique With Directly Metered Blood Flows, Circulation 19: 898, 1959.

or less, while among the last 18 patients 10 were in this age group. When age alone was considered in relation to the effectiveness of the operative treatment of secundum defects it was found that among the 9 children only 1 had a residual shunt while in the 21 adults a residual shunt was present in 7. There was no correlation between the adequacy of repair and the duration of circulatory occlusion.

In 2 patients with sinus venosus defects (D. S. and D. E.) only the interatrial communication was closed and the segmental pulmonary arteries supplying the upper and middle lobes were ligated. In each, the magnitude of the left-to-right shunt was reduced, but the residual shunt, presumably from the anomalous veins, was surprisingly large. In 2 additional patients (W. N. and M. K.), complete correction of the malformation by direct suture was attempted (Fig. 5) and was successful in 1 of them. A disadvantage of direct suture in the correction of sinus venosus defects is danger of constriction of the superior vena cava and subsequent thrombosis of it or one of the pulmonary veins. This complication was not observed, however, in either patient.

No detailed correlation was made between the clinical and hemodynamic findings at the time of postoperative study. In general, however, the presistence of fixed splitting of the pulmonary second sound was indicative of a large residual shunt. In some patients, however (for example, R. J.), normal closure of the second sound during expiration was noted postoperatively and, on the basis of the physical findings alone, the defect would have been considered completely closed.

In the latter part of the operative series, arterial indicator-dilution curves were recorded, after injection into the right superior pulmonary vein, before the thoracotomy was closed. Curves of normal contour were obtained at operation in 2 patients (C. M. and R. J.) who were later shown at catheterization to have residual shunts. It seems probable, therefore, that complete closure was initially achieved in these patients but that the suture line dehisced in the postoperative period. This view is substantiated by the findings in 2 patients with residual shunts of large magnitude who have been operated upon again with the aid of extracorporeal circulation. In each, a series of holes of varying size was present in the initial suture line. It was apparent that many sutures had torn through the septum and the initial single defect had only been converted into many smaller ones.

The primary cause for incomplete correction among the patients described is considered to be the relatively brief period of cardiotomy provided by general hypothermia. It was often difficult to define precisely the margins of the defect and direct suture was always necessary, even when it resulted in a closure under tension. In many patients there was obvious need for prosthetic replacement of a portion of the septum but the insertion of such material was patently impossible in the time allowed. Although repetitive periods of occlusion have been employed by Kirby[18] and others to extend the total period of cardiotomy, even this technique would not seem adequate for the time-consuming reconstruction

OPEN-HEART SURGERY USING DEEP HYPOTHERMIA WITHOUT AN OXYGENATOR

Archer S. Gordon, M.D., Ph.D. (by invitation), Bertrand W. Meyer, M.D., and John C. Jones, M.D., Los Angeles, Calif.

THE DEVELOPMENT of efficient heat exchangers for extracorporeal cooling of blood has now made possible prolonged intracardiac surgical procedures using deep hypothermia without a mechanical oxygenator. Detailed physiologic studies during deep hypothermia have been performed on dogs[1] and we have used it for the surgical repair of a variety of cardiac malformations. This paper reports our first 27 consecutive patients with congenital cardiac defects operated upon by this technique.

REQUIREMENTS FOR DEEP HYPOTHERMIA

Moderate hypothermia by external cooling is usually limited to temperatures of 26° to 28° C. because of the danger of cardiac arrhythmias and ventricular fibrillation below this level. There are two requirements for further cooling; (1) an efficient system for rapid cooling and rewarming of the body; and (2) a dual pump system to support the pulmonary and systemic circuits when cardiac arrest or ventricular fibrillation occur at deep hypothermic levels.

The basic equipment and hook-up for deep hypothermia is diagrammed in Fig. 1. This is essentially the same plan used by Drew[2, 3] and Kenyon,[4] in England, and Shields and Lewis[5] in this country. Systemic venous blood drains by gravity from the right atrium into a reservoir from which it is pumped back into the pulmonary circuit. Arterialized blood drains by gravity from the left atrium into a reservoir from which it is pumped through a heat exchanger and filter into the iliac artery. Occlusive roller pumps have been used and the heat exchanger is the Brown-Harrison model.[6] To produce cooling, the heat exchanger has been used in conjunction with a recirculation bucket containing crushed ice and water which maintains a temperature of between 0° and 2° C. For rewarming, hot and cold tap water are used and maintained at a temperature of 42° C. by the heat exchanger regulator. A single heat exchanger is used for patients weighing up to 80 pounds, a double heat exchanger for patients over this amount.

From the Department of Thoracic Surgery, Children's Hospital, The Hospital of the Good Samaritan, and the Department of Surgery, University of Southern California, Los Angeles, Calif.

This investigation was supported in part by U. S. Public Health Service Research Grant No. H-5248 from the National Heart Institute, U. S. Public Health Service.

Read at the Fortieth Annual Meeting of The American Association for Thoracic Surgery at Miami Beach, Fla., May 11-13, 1960.

14. Lombardo, T. A., Radigan, L. R., and Morrow, A. G.: Myocardial Failure in Experimental Hypothermia, Circulation Res. 5: 22, 1957.
15. Shumway, N. E., Gliedman, M. L., and Lewis, F. J.: Coronary Perfusion for Larger Periods of Cardiac Occlusion Under Hypothermia, J. THORACIC SURG. 30: 598, 1955.
16. Jude, J. R., Fauteux, J. P., and Harontunian, L. M.: Differential Cardiac Warming During Hypothermia, S. Forum 7: 294, 1956.
17. Bahnson, H. T., Spencer, F. C., and Neill, C. A.: Surgical Treatment of Thirty-Five Cases of Drainage of Pulmonary Veins to the Right Side of the Heart, J. THORACIC SURG. 36: 777, 1958.
18. Johnson, J., Kirby, C. K., Blakemore, W. S., and Zinsser, H. F.: Intermittent Inflow Occlusion for the Direct Visual Repair of Atrial Septal Defects, J. THORACIC SURG. 37: 314, 1959.

(For Discussion, see page 799.)

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OPERATIVE DETAILS

Metal-tipped plastic catheters are used for cannulation of the right and left atrial appendages. The left atrium is more difficult to cannulate than the right, especially if it is small or there is clockwise rotation of the heart. A plastic catheter is then inserted and secured in the pulmonary artery and a metal cannula in the iliac artery. The catheter in the pulmonary artery is usually introduced through a stab wound in an avascular portion of the right ventricular outflow tract, just below the pulmonary valve. It is threaded up through the valve and secured in place by means of a purse-string suture at the point of insertion. In the presence of severe pulmonary stenosis this catheter is inserted and secured in a similar fashion in the proximal portion of the main pulmonary artery.

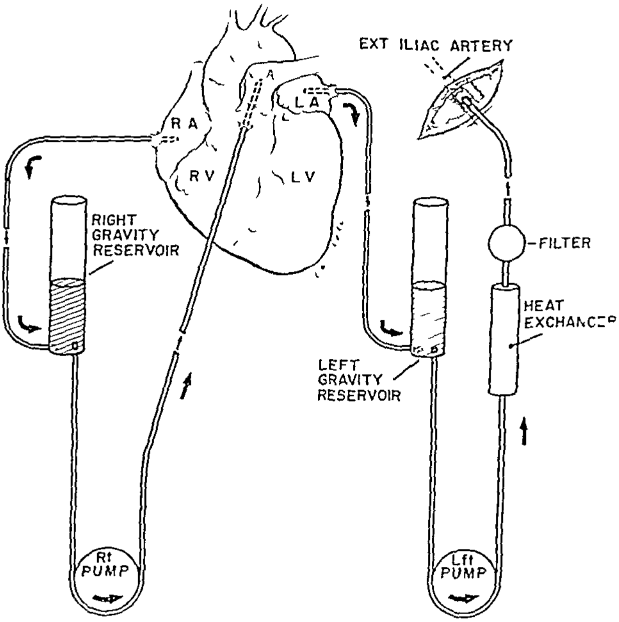


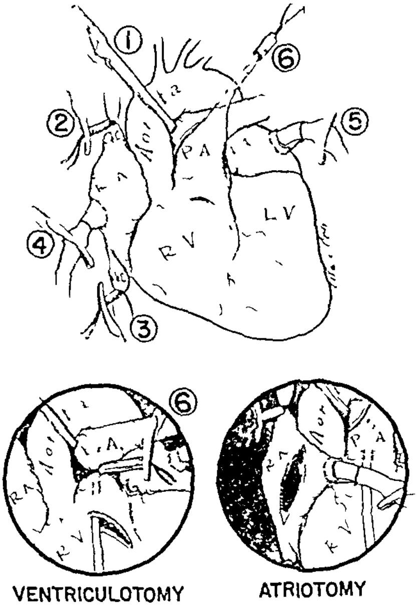
Fig 1.—Circuit and equipment for deep hypothermia

During cooling, the anesthetic agent is administered in a mixture of 95 per cent oxygen and 5 per cent carbon dioxide. When the temperature reaches 28° C., the anesthetic agent is discontinued but pulmonary ventilation is maintained.

The gravity reservoirs are adjusted for maximum drainage and the left, or systemic, circuit is started first. As soon as it is stabilized, the right, or pulmonary, circuit is activated. As the body temperature falls, the arteriovenous oxygen difference is reduced as a result of the marked decrease in oxygen consumption. The arteriovenous oxygen difference becomes negligible or absent at temperatures between 10° and 14° C.

When the body temperature has been lowered to the desired level, the pumps are turned off and the heart is isolated as illustrated in Fig. 2. The aorta (*1*) is cross-clamped for two reasons: (a) to prevent the escape of any air which might reach the left side of the heart through an atrial or ventricular defect when the right side is opened; and (b) to prevent blood from flowing back through the coronary arteries into the right heart where it would obscure the field and require aspiration. Previously placed tapes are pulled up and secured on the superior (*2*) and inferior (*3*) venae cavae.

The heart is then drained into the gravity reservoirs via the atrial catheters. The right atrial (*4*) and left atrial (*5*) lines are then clamped. The clamps on the atrial lines are not essential, but this is a useful maneuver since it prevents them from filling with air during the time the heart is open and bloodless.



VENTRICULOTOMY ATRIOTOMY

Fig 2.—Operative details for deep hypothermia

Above: Pulmonary artery catheter removed in preparation for right ventriculotomy *1*, Aortic clamp. *2*, Superior vena cava pull-up tape and clamp *3*, Inferior vena cava pull-up tape and clamp *4*, Right atrial catheter clamp *5*, Left atrial catheter clamp. *6*, Pulmonary artery pull-up tape and clamp

Lower left: Pulmonary artery catheter reinserted through the ventriculotomy and tape around pulmonary artery pulled up for filling left side of heart with blood from pulmonary pump

Lower right: Position of catheters and appendage for right atriotomy

When a ventriculotomy is performed, the catheter in the pulmonary artery is removed and the stab wound is extended for exposure of the ventricular septum. During the surgical procedure the heart remains bloodless and is completely quiet as a result of cardiac arrest or fine ventricular fibrillation. Before the final sutures of a ventricular repair are tied, the pulmonary artery catheter is reinserted through the ventriculotomy, as shown in the lower left offset of Fig. 2. The previously placed tape around the pulmonary artery (*6*) is pulled up and secured. The pulmonary circuit pump is then turned manually. This fills the left atrium and ventricle with blood, which spills over into the right ventricle. When all air has been expelled, the final sutures in the ventricular septum are tied down under blood. The pulmonary circuit is again pumped manually to test for leaks in the closure as well as for fenestrations or additional defects in the septum. When satisfactory closure has been achieved, the tape on the pulmonary artery (*6*) is released and the ventriculotomy is closed, leaving the pulmonary artery catheter in one end of the incision. Before this closure is completed, the caval tapes (*2* and *3*) are released to allow the right heart to fill with blood. The clamps (*4* and *5*) on the atrial lines are then removed and any residual air in these lines or the heart is displaced into the gravity reservoirs.

The pumps are then turned on and rewarming is started. The aortic clamp (*1*) is left in place for a minute or two during which the heart is manipulated to displace any residual air into the right or left atrial lines. The clamp on the aorta is then removed as rewarming continues.

For lesions involving the atrium, essentially the same technique is applied, except that it is unnecessary to remove the pulmonary artery catheter. The right atrial catheter is displaced to the left as shown in the lower right offset of Fig. 2 and atriotomy is performed without removal of the atrial line. The pulmonary circuit is pumped manually to exclude all air from the left side of the heart before the final atrial septal sutures are secured. Closure and rewarming are then performed in a fashion similar to the above.

For aortic or pulmonary valvular lesions, the technique is essentially the same. The pulmonary artery catheter is removed during repair of the pulmonary valve, whereas, all catheters are left in place for aortic valvular surgery.

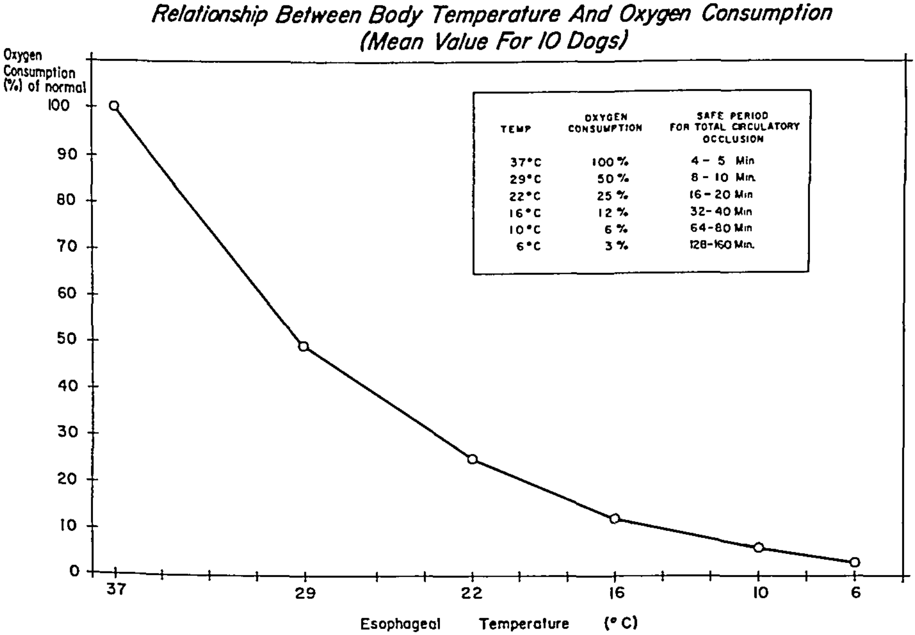
DURATION OF CIRCULATORY ARREST

Since this technique involves complete arrest of the circulation, it is essential to know the duration of circulatory arrest which can be tolerated at various temperatures without damage to the brain or myocardium.

Studies of oxygen consumption at various temperatures by Bigelow,[7] Gollan,[8] and others, have helped us in this regard. However, their studies did not include the temperature ranges in which we are interested for prolonged deep hypothermia. Therefore, we have studied the oxygen consumption in a group of 10 dogs in which the body temperature was reduced to 6° C. For these studies, the temperature and circulation were maintained at the various levels by means of extracorporeal pumps and a heat exchanger.

The results of these studies are summarized in Fig. 3. This is a simplified break-down of the data in which each point on the graph represents a 50 per cent reduction of oxygen consumption from the previous point. At 29° C., oxygen consumption is 50 per cent of normal. It is further reduced to 25 per cent at 22° C., to 12 per cent at 16° C., to 6 per cent at 10° C. and to 3 per cent at 6° C. Using the hypothesis that each 50 per cent reduction in oxygen consumption doubles the safe period for circulatory arrest, we can construct the table shown in Fig. 3. To corroborate this hypothesis, dogs have been cooled as low as 10° C. and subjected to 60 minutes of total circulatory arrest. After rewarming they made uneventful recoveries and resumed normal activities without evidence of central nervous system damage or personality alteration. These studies are reported in detail elsewhere.

These results have now been further corroborated by our clinical cases in which patients at similar temperatures have had intracardiac surgery with complete recovery to normal following circulatory arrest in excess of 1 hour.



TEMP	OXYGEN CONSUMPTION	SAFE PERIOD FOR TOTAL CIRCULATORY OCCLUSION
37°C	100 %	4 - 5 Min
29°C	50 %	8 - 10 Min.
22°C	25 %	16 - 20 Min
16°C	12 %	32 - 40 Min
10°C	6 %	64 - 80 Min
6°C	3 %	128 - 160 Min.

Fig. 3.

CLINICAL EXPERIENCES

This technique of deep hypothermia was first used by us clinically in August, 1959, for the repair of a supravalvular aortic stenosis in an 8-year-old boy. The stenosis was caused by a constriction of the aorta similar to a coarctation located 0.5 cm. distal to the aortic annulus. It was successfully repaired without creating any regurgitation by the insertion of a teflon patch in the coarcted area during 55 minutes of circulatory arrest with the body temperature at 13° C. He made an uneventful recovery and 1 year later was doing well and engaging in full normal activities.

Twenty-six additional patients with congenital cardiac defects have been operated upon under deep hypothermia since that time and are summarized in Table I. The variety of lesions in this group indicates that this modality is applicable to most congenital cardiac lesions. Only one patient with aortic valvular stenosis died and this resulted not from the use of deep hypothermia but rather from a technical error resulting in complete closure of the right coronary artery orifice in the repair of the aortotomy. The two deaths in the group having ventricular septal defects resulted from aspiration of food by one child on the third postoperative day and a complete atrioventricular block caused death on the eighteenth postoperative day in the other.

TABLE I. TWENTY-SEVEN CONSECUTIVE PATIENTS WITH CONGENITAL CARDIAC DEFECTS OPERATED UPON UNDER DEEP HYPOTHERMIA

DIAGNOSIS	NUMBER OF CASES		
	PERFORMED	RECOVERED	DIED
Atrial septal defect	3	3	
Total anomalous pulmonary veins with ASD	2	2	
Aortic stenosis			
Valvular	3	2	1*
Supravalvular	1	1	
Pulmonary stenosis			
Valvular and infundibular	2	2	
Valvular and atrial septal defect	1	1	
Valvular, infundibular, and atrial septal defect	2	2	
Ventricular septal defect	6	4	2†
Tetralogy of Fallot	7	3	4‡
Totals	27	20	7

*Technical error—Right coronary artery totally obstructed in closure of aorta.

†One VSD aspirated food on third postoperative day; other 1 died on eighteenth postoperative day with complete block.

‡One patient with tetralogy of Fallot had common ventricular chamber; 2 had absent pulmonary valve; 1 had associated ASD.

The higher mortality in the cases of tetralogy of Fallot has not been completely explained. The deaths were all in patients who had defects in addition to the usual tetralogy. One had an endocardial cushion-type of defect; 2 had congenital absence of the pulmonary valve; and 1 had an associated atrial septal defect.

The over-all mortality in this entire group of unselected cases is 26 per cent. Excluding the cases of tetralogy, the mortality is 15 per cent.

Table II summarizes the characteristics of these 27 patients and their perfusion under deep hypothermia. The lowest body temperature used was 9° C. for a patient with aortic stenosis who had 63 minutes of circulatory arrest. Most of the patients were cooled to between 10° and 14° C. The temperatures of the patients with atrial septal defects were lowered to only 20° or 21° C.

TABLE II. TWENTY-SEVEN CONSECUTIVE PATIENTS WITH CONGENITAL CARDIAC DEFECTS OPERATED UPON UNDER DEEP HYPOTHERMIA

Age	3½-26 years
Weight	29-160 pounds
Lowest temperature	9°-21° C.
Cooling rate	1.5° C. per minute
Circulatory arrest time	18-63 minutes
Temperature drift upward during circulatory arrest	
15 minutes	1°-2° C.
30 minutes	3°-4° C.
60 minutes	5°-6° C.
Rewarming rate	1° C. per minute
Blood flow rate	60-100 c.c./Kg./min.
Incidence of ventricular fibrillation	All except 3 cases

Extracorporeal cooling of blood results in more rapid and greater cooling of the "core" organs, such as the heart, brain, liver, etc., than of the great muscle and skin masses of the body. In this way it differs from external cooling in which skin and muscle are cooled first and central organs secondarily. It also differs from external cooling in that when the pumps are turned off and cooling is discontinued, the central temperature drifts upward instead of downward because the muscle mass is warmer than the core organs. This phenomenon is illustrated in Table II where it is noted that the temperature drift upward during circulatory arrest usually amounts to 1° to 2° C. in 15 minutes; 3° to 4° C. in 30 minutes; and 5° to 6° C. in 1 hour. This factor must be taken into consideration in calculating the anticipated duration of circulatory arrest. The mean temperature during this period should be used.

The flow rate depends upon the amount of gravity used and the size of the atrial catheters. Using 14 to 18 inches of gravity and either $\frac{5}{16}$ or $\frac{3}{8}$ inch catheters, the flow rates varied between 60 and 100 c.c. per kilogram per minute. These were adequate to cool the patients at a mean rate of 1.5° C. per minute. Rewarming always takes slightly longer. This would mean that cooling a patient from 37° C. to 10° C. would require 18 minutes and rewarming about 22 minutes.

As the temperature decreases, the blood flow rate also decreases as a result of increasing viscosity. However, even at the lowest temperatures, we were usually able to maintain mean blood pressures of 50 mm. Hg or over. During rewarming, the initial blood flow rate starts slowly and gradually increases as the temperature rises.

OTHER PHYSIOLOGIC DETERMINATIONS

Temperature Response.—Studies on dogs, which will be reported in detail elsewhere, have indicated the value of using esophageal temperature in these cases. We have measured skin, muscle, rectal, esophageal, brain, superior vena cava, and right gravity reservoir temperatures during cooling, circulatory arrest, and rewarming. Some of these results are shown graphically in Fig. 4. It will be seen that the esophageal and brain temperatures drop rapidly during cooling, drift up almost the same amount during arrest, and rise rapidly during rewarming. In these studies, the esophagus was usually about 1° C. warmer than the brain, although it was occasionally a degree cooler. This means that accurate monitoring of the esophageal temperature provides an index of brain temperature, plus or minus one degree. Rectal temperatures, even after cleansing enemas, failed to parallel esophageal temperatures closely. The lag in muscle temperature change is also shown in the diagram, and its influence on the upward drift of brain and esophageal temperature during circulatory arrest is obvious.

The esophageal temperature usually drifted upward more than the brain temperature. This is probably an anatomic effect, since the core organs in the trunk are surrounded by a generous muscle and subcutaneous mass, whereas, the brain is more isolated and the drift of the temperature tends to be less.

At the completion of rewarming to temperatures of 36° to 37° C. the esophageal temperature always drifts downward several degrees since the muscle mass remains cooler than the core organs.

Electrocardiographic Responses.—Ventricular fibrillation occurred in all except 3 of the patients. In these latter cases, a normal rhythm resumed spontaneously. Ventricular fibrillation usually occurred below 18° C., although occasionally at higher temperatures. Those hearts which did not fibrillate during cooling, usually went into ventricular fibrillation during the surgical procedure. However, the cooler the temperature, the finer is the fibrillation. During cardiotomy, if ventricular fibrillation is present it is so fine that there is no gross movement and it can only be detected on the electrocardiogram. Most of the hearts followed a characteristic electrocardiographic pattern which included early premature ventricular contractions, followed by atrial fibrillation and progressing into bradycardia, coarse ventricular fibrillation and, ultimately, fine ventricular fibrillation (Fig. 5). During the period of circulatory arrest, the heart frequently changed back and forth between ventricular fibrillation and cardiac arrest, with an occasional electrocardiographic complex.

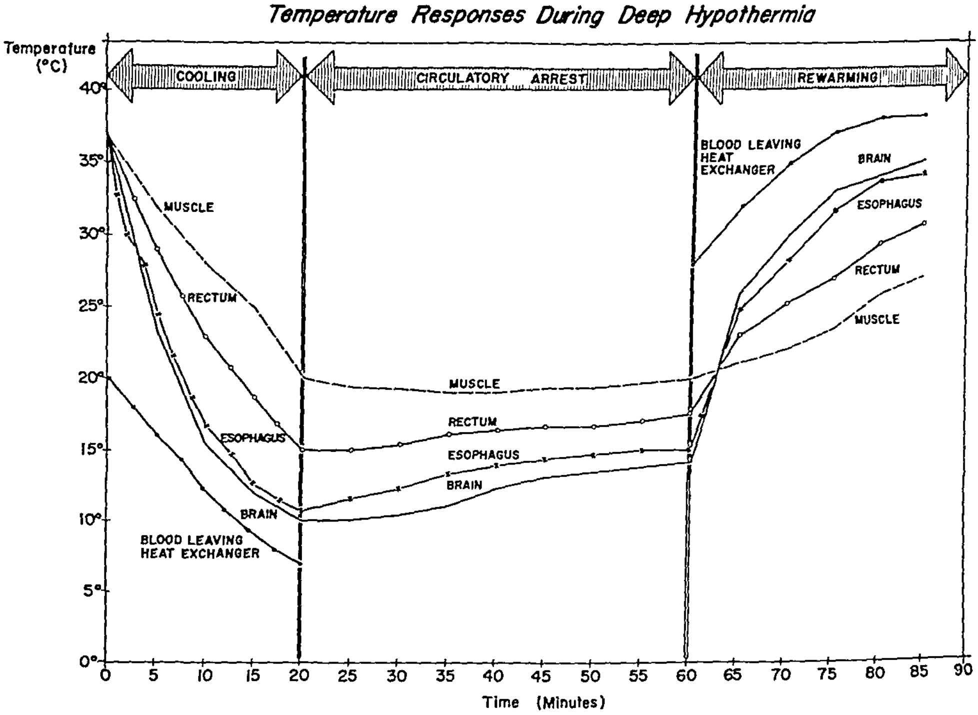

Temperature Responses During Deep Hypothermia

Fig. 4.

Rewarming usually initiated a fine fibrillation which gradually became more coarse. The hearts were defibrillated when the temperature reached 30° C. Most of them were defibrillated with a single shock. The heart with the right coronary artery sutured closed required three shocks, and one other heart required two shocks.

Electroencephalographic Response.—All of the patients had preoperative and postoperative complete electroencephalograms. All of these were read as normal. There was no evidence of any neurological, central nervous system, personality, or behavior alteration in any of these cases.

Electroencephalograms taken during the procedures usually followed a characteristic pattern (Fig. 6). During the early stages of cooling, alpha activity increased perceptibly but, later, slowed and large delta waves appeared. Below 16° to 18° C., activity almost ceased, although some very fine waves persisted. However, these probably represent artifacts, such as the activity of the pumps or electrical potential in the skin, rather than brain waves. The electroencephalogram remained completely flat during circulatory arrest. It

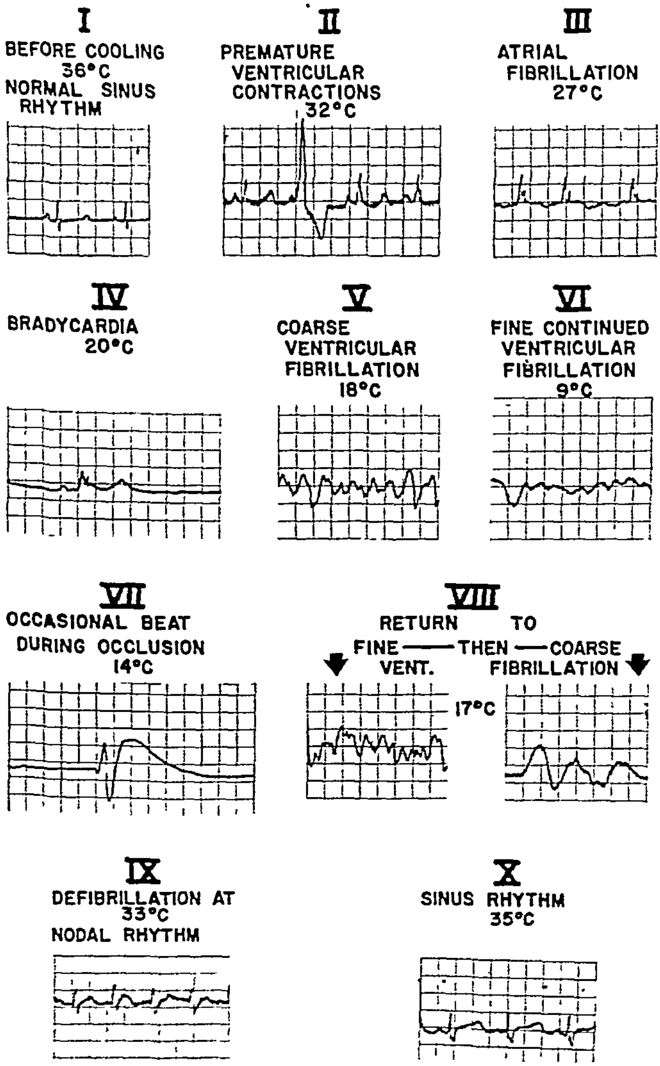


Fig 5.—Electrocardiographic response to deep hypothermia.

was re-activated during rewarming, but the patterns returned much more slowly than they had disappeared during cooling. In fact, the electroencephalogram lagged far behind the brain temperature in returning to normal. This was a common finding for which we have no explanation. However, the electroencephalogram was back to normal within 20 to 40 minutes after rewarming had been completed.

Metabolic Effects.—The metabolic responses during and after 2 typical cases of deep hypothermia are summarized in Table III. There were no significant changes in arterial or venous pH, CO_2 content, lactic acid, or pyruvic acid during cooling to 10° C All pH samples were run at the same temperature

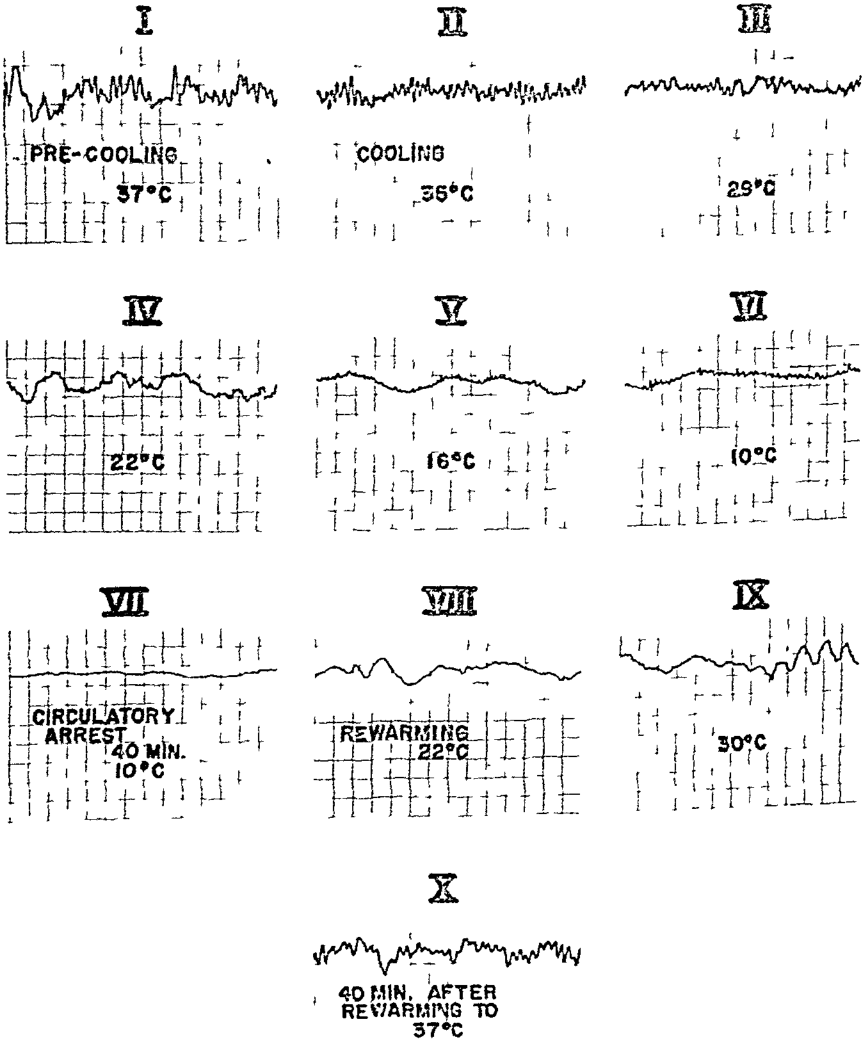


Fig 6 —Electroencephalographic pattern during deep hypothermia

at which they were drawn. This is essential since temperature change affects hydrogen ion dissociation and acidotic readings will be obtained if determinations are made at standard temperature.

TABLE III. METABOLIC EFFECTS OF DEEP HYPOTHERMIA, CASES 24 AND 25 (MEAN VALUES)

TIME OF DETERMINATION	pH		CO_2 CONTENT (MEQ./L.)	LACTIC ACID (MG. %)	PYRUVIC ACID (MG. %)
	ARTERIAL	VENOUS			
Before cooling	7.49	7.42	16	14.7	0.57
During cooling					
22° C.	7.46	7.42	18		
16° C.	7.46	7.42	17		
10° C.	7.44	7.40	19	20.1	0.54
Start rewarming	7.24	7.22	12	28.8	0.57
Finish rewarming	7.29	7.23	11	35.0	0.82
Postoperative					
2 hr.		7.28	14	32.8	0.41
8 hr.		7.32	19	14.5	0.64
24 hr.		7.34	22	16.3	0.54
48 hr.		7.36	23	17.3	0.68

Diagnosis: Ventricular septal defect.
Circulatory arrest: 40 minutes.
Lowest temperature: 10° C.

During rewarming the pH became somewhat acidotic. This resulted from the flushing out of acid metabolites which had accumulated in the tissues during circulatory arrest. The drop in buffer base and the rise in lactic acid during rewarming are responsible for the pH change.

Within 2 hours after surgery, all metabolic determinations were returning to normal and, by 8 hours, they had reached normal ranges, where they remained. The pyruvic acid rose somewhat during the rewarming phase, but it remained within normal limits throughout the procedure.

Postoperatively these patients did not appear acidotic and none of them required any alkaline medication.

ADVANTAGES OF DEEP HYPOTHERMIA

During the past several years it has become increasingly evident that successful intracardiac surgery can be performed using various techniques and various types of equipment. Some groups have even found it advantageous to combine several methods, such as deep hypothermia with a pump-oxygenator.[9-12] It would appear that results are related not to the specific technique or equipment used but, rather, to the background and experience of the pump team, to the type and severity of cases selected for open-heart surgery, and to the skill and experience of the surgeon.

Accordingly, a change to the use of deep hypothermia should be based upon distinct advantages that it offers over other methods for open-heart surgery. We believe its advantages are threefold: (1) mechanical simplicity, (2) reduced blood volume, and (3) an ideal operative field.

The mechanical simplicity speaks for itself. The elimination of the oxygenator with its adjuncts and monitoring devices not only has simplified the was re-activated during rewarming, but the patterns returned much more slowly than they had disappeared during cooling. In fact, the electroencephalogram lagged far behind the brain temperature in returning to normal. This was a common finding for which we have no explanation. However, the electroencephalogram was back to normal within 20 to 40 minutes after rewarming had been completed.

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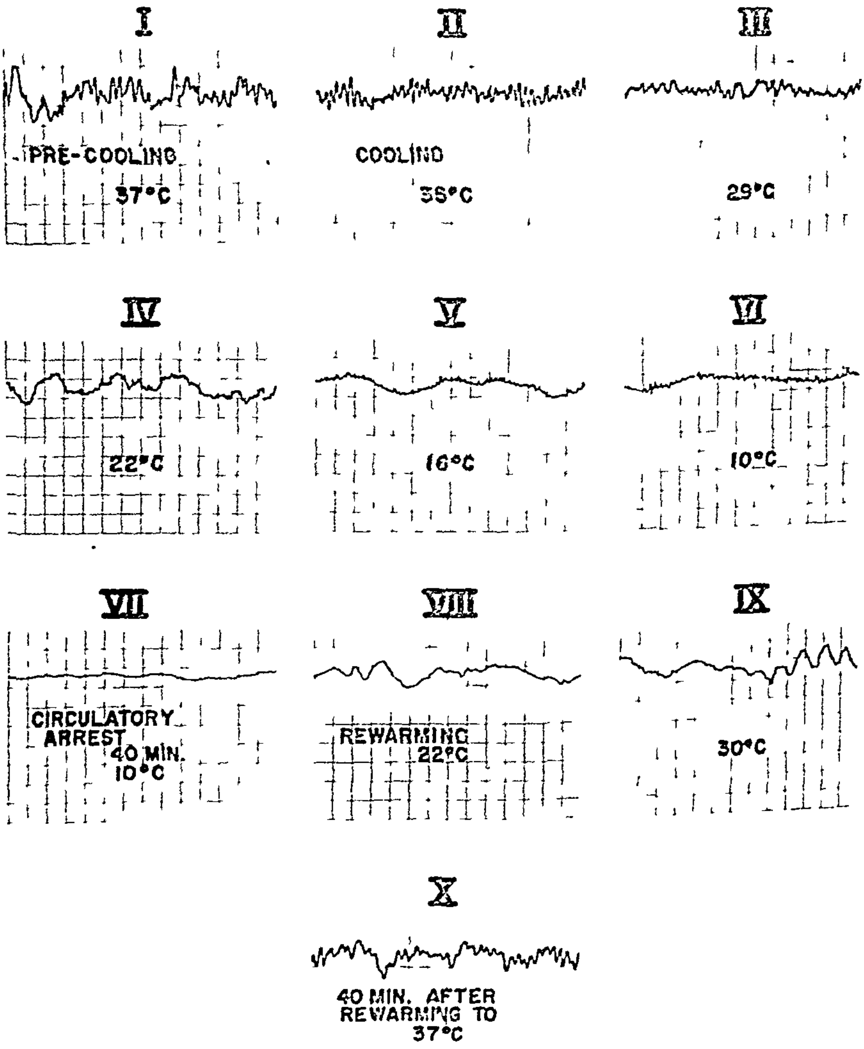

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Circulatory arrest: 40 minutes.
Lowest temperature: 10° C.

During rewarming the pH became somewhat acidotic. This resulted from the flushing out of acid metabolites which had accumulated in the tissues during circulatory arrest. The drop in buffer base and the rise in lactic acid during rewarming are responsible for the pH change.

Within 2 hours after surgery, all metabolic determinations were returning to normal and, by 8 hours, they had reached normal ranges, where they remained. The pyruvic acid rose somewhat during the rewarming phase, but it remained within normal limits throughout the procedure.

Postoperatively these patients did not appear acidotic and none of them required any alkaline medication.

ADVANTAGES OF DEEP HYPOTHERMIA

During the past several years it has become increasingly evident that successful intracardiac surgery can be performed using various techniques and various types of equipment. Some groups have even found it advantageous to combine several methods, such as deep hypothermia with a pump-oxygenator.[9-12] It would appear that results are related not to the specific technique or equipment used but, rather, to the background and experience of the pump team, to the type and severity of cases selected for open-heart surgery, and to the skill and experience of the surgeon.

Accordingly, a change to the use of deep hypothermia should be based upon distinct advantages that it offers over other methods for open-heart surgery. We believe its advantages are threefold: (1) mechanical simplicity, (2) reduced blood volume, and (3) an ideal operative field.

The mechanical simplicity speaks for itself. The elimination of the oxygenator with its adjuncts and monitoring devices not only has simplified the system, but has completely eliminated such problems as siliconizing, foaming, level control, flow control, and hemolysis. The use of hypothermia has made it possible to stop the pumps at any time during the cooling or rewarming for whatever eventuality may arise.

The total priming volume for the complete system is 1,200 c.c. of heparinized blood. This volume is the same for all patients, except for the addition of 150 c.c. when a second heat exchanger is used for patients over 80 pounds. Careful attention to consolidation of the equipment and shortening of the plastic flow lines should allow this to be reduced to 1,000 c.c., so that two pints of heparinized blood will suffice for priming the system.

There are a number of factors which contribute to providing an ideal operative field. (1) The isolated, drained heart is completely bloodless. When clamped off and drained, as illustrated in Fig. 2, a constant dry field is provided. Since no blood is flowing during the surgery, neither coronary flow, augmented bronchial return, nor the presence of a persistent left superior vena cava or a patent ductus arteriosus can obscure the field with blood. Only a minimal amount of blood need be aspirated when the heart is first opened, and this may be discarded or reused, as desired. (2) The operative field is completely quiet from cardiac arrest or fine ventricular fibrillation without the need for cardioplegic drugs, anoxia, or injections of cold blood. (3) No one but the surgeon who has performed open-heart surgery with a pump-oxygenator operating throughout the procedure can truly appreciate the blessing of having no equipment operating while he is working inside of the heart. He can devote his undivided attention to the surgery without any misgivings about the disastrous effects of equipment or personnel failures during the perfusion. Also, during the cooling and rewarming period, he is not busy doing surgery and can devote his attentions to this part of the procedure if necessary. (4) Since the heart is not beating and the aorta is clamped off throughout the intracardiac procedure, there is minimal danger of air embolism. We have seen no evidence of air embolism in these 27 cases. Careful filling of the chambers, as well as the vents provided by the right and left atrial catheters, further reduces this danger at the completion of the surgical repair.

An additional feature worthy of mention is that more time can be provided for further surgery, if required, at the completion of the safe period for circulatory arrest. Re-perfusing and recooling until the venous blood again becomes arterialized and the temperature reaches the desired level makes it possible to extend the period of circulatory arrest by a significant amount. In 2 cases of severe infundibular obstruction, when rewarming was started after completing the infundibulectomy and closing the right ventricle, bright red blood streaming out of the right atrial catheter indicated the presence of an undiagnosed atrial septal defect. These patients were recooled and perfused briefly, following which their atrial septal defects were closed and they made uncomplicated recoveries. One other patient with total anomalous pulmonary venous drainage and a large atrial septal defect was re-perfused and recooled between correction of the venous drainage and closure of the atrial septal defect.

COMMENT

Many modalities and techniques are available for the successful intracardiac repair of congenital cardiac defects. Deep hypothermia has been used by us successfully on a variety of such lesions and appears to offer definite advantages. For some lesions we will still probably desire a beating heart and the use of a pump-oxygenator. Further experiences should delineate more clearly the role of deep hypothermia and the patients who will profit most by its use.

REFERENCES

1. Gordon, A. S., Jones, J. C., Luddington, L. G., and Meyer, W. B.: Deep Hypothermia for Intracardiac Surgery: Experimental and Clinical Use Without an Oxygenator, Am. J. Surg. 100: 332, 1960.
2. Drew, C. E., and Anderson, I. M.: Profound Hypothermia in Cardiac Surgery: Report of Three Cases, Lancet 1: 748-750, 1959.
3. Drew, C. E., Keen, G., and Benazon, D. B.: Profound Hypothermia, Lancet 1: 745-747, 1959.
4. Kenyon, J. R., Ludbrook, J., Downs, A. R., Tait, I. B., Brooks, D. K., and Pryczkowski, J.: Experimental Deep Hypothermia, Lancet 2: 41-45, 1959.
5. Shields, T. W., and Lewis, F. J.: Rapid Cooling and Surgery at Temperatures Below 20° C., Surgery 46: 164-174, 1959.
6. Brown, I. W., Jr., Smith, W. W., and Emmons, W. O.: An Efficient Blood Heat Exchanger for Use With Extracorporeal Circulation, Surgery 44: 372-377, 1958.
7. Bigelow, W. G., Lindsay, W. K., Harrison, R. C., Gordon, R. A., and Greenwood, W. F.: Oxygen Transport and Utilization in Dogs at Low Body Temperature, Am. J. Physiol. 160: 125, 1950.
8. Gollan, F.: Electrolyte Transfer During Hypothermia *in* The Physiology of Induced Hypothermia, edited by R. D. Dripps, Washington, D. C., 1956, National Academy of Science—National Research Council, pp. 37-41.
9. Pierce, E. C., Dabbs, C. H., Rogers, W. K., Rawson, F. L., and Tomkins, R.: Reduced Metabolism by Means of Hypothermia and the Low Pump Oxygenator, Surg. Gynec. & Obst. 108: 339-352, 1958.
10. Young, W. G., Jr., Sealy, W. C., Brown, I. W., Jr., Smith, W. W., Callaway, H. R., Jr., and Harris, J. E.: Metabolic and Physiologic Observations on Patients Undergoing Extracorporeal Circulation in Conjunction With Hypothermia, Surgery 46: 175-184, 1959.
11. Lesage, A. M., Sealy, W. C., Brown, I. W., and Young, W. G.: Hypothermia and Extracorporeal Circulation, A. M. A. Arch. Surg. 79: 607-613, 1959.
12. Sealy, W. C., Brown, I. W., and Young, W. G.: A Report on the Use of Both Extracorporeal Circulation and Hypothermia for Open Heart Surgery, Ann. Surg. 147: 603, 1958.

DISCUSSION

(PAPERS BY SCANNELL [PAGE 723], MULDER [PAGE 731], HARKEN [PAGE 744], KIRKLIN [PAGE 763], MORROW [PAGE 776], GORDON [PAGE 787], AND THEIR ASSOCIATES)

DR. DWIGHT F. HARKEN, Boston, Mass.—About 10 years ago Dr. Laurence B. Ellis realized that we were going to perform a lot of operations for mitral stenosis, so he set up a program for following these patients. He and his associates with the help of one to three full-time workers have carried this study through the years. I'd like to say a few things about this follow-up. This work has been reported periodically and largely supports Dr. Scannell's comments.

We are now in our third thousand operation on the mitral valve. The follow-up discussion today involves the first thousand.

The mortality rate has not been dissimilar to Dr. Scannell's. In ideally selected patients, the Group III patients of our classification, there was a mortality of less than 1 per cent. In the Group IV category, it was 21 per cent. Dr. Scannell used the medically treated patients of Drs. White, Bland, and Sprague for comparison with his surgical results.

We used Olesen's medical series. The series of Drs. White, Bland, and Sprague is quite similar to Olesen's and to current medical treatment. At the end of 9 years, 75 per cent of the Group III patients (those with predominantly progressive pulmonary symptoms) were alive, whereas there was only 40 per cent survival in a similar group treated medically.

Of those in refractory congestive failure (our Group IV), 60 per cent of the surgically treated patients survived after 9 years, whereas all of the medical control group were dead within 8 years. And gentlemen, survival is only a cold parameter of living, for among the surgical survivors there was much more happiness, comfort, and rehabilitation. The implications in patient selection are obvious. They should be operated upon when they are in Group III which has less than 1 per cent mortality and high rehabilitation rates.

Now I should like to take a slightly different point of view to illustrate a point that I'm sure Dr. Scannell has made, but I should like to make it in a slightly different way.

We don't have to prove to ourselves that surgery is useful, but we do want to know if and why these people deteriorate after being improved by surgery. In our first thousand patients, Dr. Ellis' group finds that there are 228 patients who are now, or were at the last review, less well than at some other time since operation.

Now this doesn't mean that surgery wasn't worth while, or even lifesaving, but 228 of them are now less well than they were at some time since operation. This is the important group for us to scrutinize to appreciate a point of view that Gordon is trying to emphasize.

There were four dominant overlapping factors responsible for this deterioration, and I emphasize "overlapping." The first and overwhelming one was what we would now term unsatisfactory initial operation—more than half the patients; second, recurrent rheumatic fever; third, mitral insufficiency prior to or caused by operation; fourth, multivalvular disease.

As for the unsatisfactory operation, this thousand was operated before we recognized the importance of opening the posteromedial commissure. Dr. Bailey has suggested the right thoracotomy to make this possible. I move around to the opposite side of the table in the standard left thoracotomy. Logan, Tubbs, Gerbode and others use a transventricular valvulotome. It is not so important how it's done as it is to recognize what must be done, and do it. Thus, I think we now take care of this factor in deterioration by more satisfactory initial (or secondary) operation.

The second factor, rheumatic fever, probably is less significant since the advent of routine permanent prophylaxis with antibiotics and the appropriate use of steroids. When this group was operated upon, routine permanent penicillin prophylaxis was not practiced.

The other two categories, mitral insufficiency and associated valvular disease, resolve themselves into better diagnosis and the appropriate rather than the inappropriate operations. When this group of patients was operated upon we had less satisfactory clinical and laboratory diagnostic techniques (left heart catheterization, etc.) and no adequate techniques for dealing with some of the lesions. There was no good operation for aortic stenosis and mitral insufficiency, much less aortic insufficiency, so we simply did the best we could with the mitral stenosis and hoped that the associated disease was insignificant. That can be changed now.

In conclusion, most causes of deterioration can be handled better now. Most importantly, we cannot only operate better initially but, by using the same principles at reoperation with an operating tunnel, we can make reoperation just as satisfactory as the modern improved primary procedure with bicommissural and subleaflet valvuloplasty.

In the light of this knowledge, when I hear talk about routine open operation for initial or reoperation, it worries me. Just because we have a pump-oxygenator, we don't have to use it. We don't have to use a bulldozer to mow the lawn. You reserve the bulldozer for the stumps, and if you use the mower well, it's surprising how few stumps there are.

DR. SCANNELL (Closing).—I don't know whether I should just close or ask Dr. Harken if I might discuss his paper.

Obviously, there is considerable agreement. I think the important thing for us to decide is: how to know that the stumps are going to be there, and use an open approach the first time around under these conditions, which I rather favor

Second, it is important to recognize the break in compensation that occurs in these patients and, when they are getting into trouble, reoperate early

I did not have time in the original paper to talk very much about this problem of reoperation As we see it, we have been too reluctant to readvise surgery We have operated upon patients after their lungs were badly damaged with severe arterial disease and, under these circumstances, end up with an excellent valve—but at autopsy.

DR CHARLES P. BAILEY, New York, N Y—In view of the skepticism that greeted my first presentation of a somewhat similar technique to this Association 2 years ago, I am delighted to see that Dr. Mulder and others have done this type of operation and are getting good results

(Slide) In fact, as I remember, the procedure was referred to as an "explosion in a cement factory" on that occasion.

(Slide) Over the past several years we have been doing open heart surgery for acquired aortic stenosis. We did use hypothermia alone in some patients but gradually have come to depend upon complete bypass with coronary artery cannulation and perfusion, with or without the addition of hypothermia. We have had a mortality as shown in this latter group in 52 cases of 11 5 per cent. Generally the postoperative results have fitted as well with the later ones shown by Dr. Mulder

(Slide) Louis Gross in 1936 showed the double layer make up of the thin, transparent aortic valve (laminum spongiosum and laminum fibrosum), which permits the application of such a technique as Dr. Mulder has so beautifully demonstrated However the lesion, as he pointed out, may not be limited to the concave aspect of the valve although it usually is

It is true that one should mobilize the cusps by separating the commissures whenever feasible In this photograph, this cusp, however, can be seen to be a shallow one, and this one is even more shallow. Had we done an open operation in this case, it might have been well to mobilize only this deeper cusp, to have separated it at the commissures, allowing the remaining two to be joined in a rigid shelf which would support itself if only by virtue of its attachment to two thirds of the aortic circumference A good clinical result will be obtained even if only one cusp functions well

(Slide) This slide merely shows the reparative technique that we have used in preference to using a plastic or prosthetic cusp A segment of free aortic wall is used to create a new cusp after excising an extremely damaged one

I have a one minute movie which can be shown, demonstrating our technique

DR DWIGHT C MC GOON, Rochester, Minn—Dr Mulder has nicely demonstrated his enthusiasm for the surgical treatment of calcifying acquired aortic stenosis, and, of course, Dr. Bailey shares that enthusiasm with him So also do I

I think it is understandable that when a condition for which there was no suitable treatment until 2 or 3 years ago becomes amenable to the surgeon, we should be enthusiastic about the prospect Perhaps future follow up studies will show that our optimism is not warranted, but perhaps also by that time newer techniques will have become available

You recall that Dr. Kirklin reported upon 14 of our patients—the first 14—some time ago, among whom there was one early death and one late death. The series has now increased to 41 patients, with the mortality rate remaining at approximately 10 per cent. The only feature of the original technique which might be different in view of contemporary developments is that we used normothermia throughout the series We have merely cross clamped the aorta, and usually have begun to work on the left coronary cusp first After

15 or 20 minutes have passed, work on this cusp is completed, and we then begin perfusion of the left coronary artery with about 400 c.c. of normothermic blood per minute. The heart very rapidly resumes its action, and usually it is possible to continue that perfusion throughout the remainder of the period of repair of the valves.

I think the most important feature of the technique is to be able to work in an unhurried manner, and not to feel the press of time. Work on the valves not uncommonly may continue for an hour or more.

By this means, when the aortic clamp is removed, the heart is oxygenated and as it has been vigorously contracting for a prolonged period, it is quite able to take over the circulation, even if a minor degree of aortic insufficiency should be present.

DR. JOHN F. BURKE, Boston, Mass.—We too have been interested in acquired aortic stenosis at the Massachusetts General Hospital, and have now done 42 operations; the last 25 patients have survived.

(Slide) We have noted that the more of these operations we do, the longer it takes us. We have used moderate hypothermia without coronary perfusion and, although we do not mean to imply that cardiac ischemia is good cardiac muscle, it is obvious that there are other factors which are perhaps even more important than perfusion of the coronaries. We believe one factor is an excellent restoration of valve function. Although coronary occlusion and ischemia was carried out in our cases, the results became better as we took a longer time to achieve a valve that would function almost perfectly.

DR. CLARENCE CRAFOORD, Stockholm, Sweden.—I would like to draw your attention to one point.

Dr. Scannell said that if there was a gradient over the valve of less than 50 mm. Hg, he did not think that these patients were candidates for surgery. I think that in the case of aortic stenosis one should not only evaluate the gradient when the patient is resting. One should also evaluate the gradient at work and after work.

We have had patients with gradients as low as 20 or 30 mm. Hg after measured work. At rest, with one catheter in the left ventricle and one in the ascending aorta, the gradient might well rise to well above 100—up to 200 mm. Hg, and I think these patients are candidates for surgery as well.

DR. MULDER (Closing).—I should like to emphasize one point that we think is very important; namely, that it is better to start the dissection of the calcium at the base of the cusp and move centrally, rather than cutting blindly across the top of the encrustations.

With regard to Dr. Crafoord's remarks, we would certainly agree that the cardiac output varies under certain circumstances, and that this may alter the gradient measured across the aortic valve. We have operated on 1 patient with a low cardiac output and a gradient of less than 50 mm. Hg. He has had a very good result which suggests that in those patients with a low output, the demonstration of a gradient, even though less than the arbitrary 50 mm. Hg, may still be indication for operation.

DR. DONALD B. EFFLER, Cleveland, Ohio.—At the 1958 meeting of this Society in Boston, we discussed the need and our interest in prosthetic replacements of the aortic and mitral valve. Since that time Dr. Willem J. Kolff of the Cleveland Clinic Foundation has devoted considerable energy toward prosthetic valve replacement. Utilizing an excellent laboratory and applying the patience and energy characteristic of the indomitable Dutch, he has explored many facets of this complex field. I would like to show a short movie that demonstrates a number of significant experimental observations.

This is a Teflon mitral valve replacement; the dog died 10 days after operation. Viewed from the ventricular side it is self-evident that the prosthesis has become a thrombus factory. The animal died of multiple emboli.

This specimen is another mitral prosthetic replacement. The animal survived 4 weeks after operation and then developed a classical picture of mitral stenosis. This is not an isolated experience; unless the animal receives anticoagulants or fibrolysin materials, stenosis inevitably occurs in this type of valve.

This is an aortic monocusp replacement—the animal died with a large saddle embolus. The monocusp (polyurethane in this instance) contains an impaction of thrombus 14 days after insertion.

Dr. Kolff has worked with most of the available plastic materials and used all conceivable variations including the woven, knitted, smooth, and roughened types. The record of initial animal survivors after complete valve replacement has been excellent—the long-term survival rate is discouraging.

The concluding specimen is of particular interest. A Teflon strip has been fixed to the right atrial septum and dropped through the tricuspid valve where it is attached to the apex of the right ventricle. All dogs survived this simple procedure, but all succumbed at a later date when the atrial chamber follows the prosthetic strip and invaginates into the tricuspid valve in a manner reminiscent of a toilet plunger. Apparently there is an unexplained taxis phenomenon here.

The purpose of this film is obvious. It is not our desire to be distributors of sodden blankets. We all know that there are many perplexing and discouraging problems in this particular field—that, for the present, clinical application of prosthetic valve replacement at either the mitral or aortic level must be undertaken with considerable caution. For the present it is our policy in the surgical treatment of aortic and mitral valve disease to do the best we can with what the patient has. This policy will remain in force until we can provide our patients with better prosthetic valves than are available to us now.

DR. EARLE B. KAY, Cleveland, Ohio.—Whereas not over 10 to 15 per cent of the patients with mitral regurgitation require valvular substitution, it is our opinion that the majority of patients with aortic regurgitation and at least 50 per cent of patients with highly destroyed calcific stenotic valves will require valvular replacement for optimal correction.

The success of aortic valvular surgery is dependent upon three factors: (1) complete correction of the insufficient valve which assures, rather than hopes for, maximal or optimal valvular function; (2) proper myocardial support and management during and immediately following perfusion, and (3) a left ventricular myocardium that will tolerate the operative procedure.

During the past 4 years we have, as many of you also have, gone through the many intervening stages of partial or palliative correction of the insufficiency employing valvular addition, monocusps, plication, or excision of the noncoronary cusps, and the many other variations in techniques and have been impressed with the fact that, although occasional spectacular results were obtained with the above techniques, we were never assured at the time of the operative procedure that adequate or ideal correction had been accomplished.

Ideally, one must be assured at the time of the operative procedure that the insufficiency is entirely corrected and that no stenosis is produced. In our opinion this can only be accomplished by valvular substitution with a plastic tricuspid valve.

One hears the criticism that perhaps there is insufficient knowledge of the destiny of such valves but in actuality the only difference between a complete tricuspid valve and a monocusp or plastic used in valvular addition is the degree and design rather than the substance. The majority of the plastics appear well tolerated and have been used in various forms for 2 to 3 years. Furthermore, a tricuspid valve assures deep sinuses of Valsalva and proper coaptation of the leaflets. The high operative mortality in the past has been due to incomplete valvular correction and insufficient myocardial support and management during the procedure.

In regard to myocardial support, we have all had what we felt was a satisfactory correction of the insufficiency only to be confronted with a heart difficult to start, or to fail later because of the prolonged anoxia or inadequate myocardial oxygenation occurring during the period the aorta is cross-clamped. We have employed all of the current techniques for myocardial management during the period of cross-clamping the aorta and continue to feel that direct coronary artery perfusion, as described to this Society 2 years ago, is superior to other techniques if operating periods up to 1 or 2 hours are required. Shorter periods of aortic cross-clamping are well tolerated with cardiac arrest by perfusion of ice-cold Ringer's solution. Recently we used the combination of cardiac arrest by coronary perfusion of oxygenated ice-cold Ringer's solution to cover the 10- to 15-minute period to establish coronary cannulation, followed by direct coronary perfusion with oxygenated blood during the insertion of a plastic tricuspid aortic valve. The postoperative recovery of this patient was the most benign of any operated upon. We continue to use both left and right atrial decompression during the operative period as well as during the immediate post-perfusion period.

DR. WILLIAM H. MULLER, JR., Charlottesville, Va.—I, too, agree that in repairing the valves in patients with hypertrophied, dilated ventricles one must relieve the insufficiency without increasing the resistance at the site of the valve.

We make every effort to use the patient's own tissues in repairing aortic insufficiency but, in some instances, this is not possible and we utilize leaflet replacement or leaflet extension, and also total valve replacement.

I would like to present a very short filmstrip demonstrating a Teflon valve that we inserted in an 18-year-old patient who had aortic insufficiency as a result of bacterial endocarditis.

The extreme pulsation of the aorta is apparent. The aorta was clamped and an incision was made into it in a way similar to that demonstrated by Dr. Mulder. The posterior leaflet was completely absent except for a small tag, and there were multiple perforations in the two remaining leaflets. It was decided to replace the valve totally in this patient.

We, therefore, excised the remaining leaflets, leaving a small portion along the rim to which the prosthesis could be anchored. The sutures were placed through the tough, thick annulus, and also in the prosthetic valve. (The prosthetic valve had a Teflon cage covered with Teflon netting. The inside is polished, and the leaflets are knitted Teflon with polyurethane-treated edges. The cage is cut out to accommodate the region of the coronary artery orifices.)

The valve was positioned and additional sutures were placed around the top of the valve. We utilized coronary perfusion of the left coronary artery, and we have been using it in the right coronary artery while we are closing the aorta. The pulsations of the aorta which were formerly present were greatly diminished.

This patient was operated upon about 5 weeks ago and is doing satisfactorily. We don't believe that this valve is the answer, but we hope that it's a step in the right direction. Many questions must be answered regarding the long-term fatigue properties of Teflon. Certainly, stiffening of the leaflets as Dr. Effler showed a moment ago and a number of other points will have to be considered. None of the patients in whom this valve was used has presented any evidence of emboli. We have totally replaced the valve in 5 patients, 2 of whom are still doing satisfactorily; 1 early and 1 about 18 months since operation. All of these patients had severe aortic insufficiency and, at the time of operation, it was believed that total replacement was necessary to enable them to survive the perfusion.

DR. ALFRED GOLDMAN, Beverly Hills, Calif.—I want only to bring out a few points that haven't been brought out relative to the use of autogenous tissue in aortic insufficiency.

Aortic insufficiency may at times be caused by a prolapsed cusp (Slide) The anatomy of prolapse is depicted diagrammatically here This cusp prolapses because of weakness of the supporting strut made up by the spongiosa, annulus fibrosa, and aortalis as they form the strut for the coapting ridge, which in its center contains the nodulus arantii all three of which must meet at a single point to produce a competent valve

(Slide) This weakness of the strut support to the cusp close to the aortic wall produces the sagging of the lunula and a disalignment of the noduli arantii on closure of the valve in diastole, so that it becomes incompetent

(Slide) This slide diagrammatically depicts the physiology of the prolapsing valve on diastole This incompetent space remains Therefore, the point of attack is this anatomic area of the valve close to the aortic wall, in order to splint the sagging lunula on the well lunula by a supporting strut made with a free arterial graft taken from the internal mammary artery

(Slide) The technique shown on this slide has been utilized in a 46 year old man with severe aortic insufficiency and a prolapsed cusp, who was operated on 18 months ago and who at the present time has improved radial arterial tracings He had not worked for a year and a half, and he has been able to work for the past year Diastolic pressure was raised from 20 to 60, and his cardiac size is smaller than it was preoperatively The strutting material was autogenous arterial segment taken from the internal mammary artery

We have found in dogs that free arterial segments, when planted in the myocardium the endocardium, or in the valve itself, are well tolerated, and in periods of time up to 16 months these free arterial grafts tend to harden and become supportive

DR HARKEN (Closing) —Dr Effler's observations are timely, and we too have feared stiffening and contraction of materials that become organized as scar tissue This is why we have been reluctant to use wettable materials However Dr Muller's experience suggests that some of our fears are unnecessary I hope he's right It would simplify the problem At least our caged ball valve does not have some of these potential disadvantages Perhaps it will have disadvantages of its own

I agree with most of the fine points made by Dr Kay and appreciate his emphasis on the importance of avoiding stenosis Here again you get the undertone of alarm in all of these discussions about aortic insufficiency with its dilated ventricle in failure

Dr Muller's brilliant cases warrant his enthusiasm and our commendation I noticed that he was perfusing only one coronary artery One cannot argue with success but I believe that if one is good, two are better A substantial part of the left ventricle is perfused by the right coronary artery, therefore we should perfuse it as well as the left

Dr Goldman's comments about the prolapsed cusp represent excellent observations It was no coincidence that his diagram showed prolapse of the noncoronary bearing cusp As a mater of fact, that concept was the basis for our circumclusion operation although I admit that it has been less than dramatically successful It was also the basis for the first anatomic drawing that I showed today in which the base of the aorta was dilated and the neutral cusp had prolapsed downward and backward Aortic insufficiency in these situations is a two dimensional affair one transverse and another longitudinal I would be a little wary of producing stenosis whenever suturing commissures together, but obviously he was wary and successful

As usual, a paper presented to this Society has flushed out a lot of valuable information From you I have learned a lot As the expression goes thanks for letting me bring the can opener to the picnic

DR HENRY T. BAHNSON, Baltimore, Md.—This is the usual loaded concise forthright Kirklin presentation on which I would like to compliment him and make a few comments about one small segment of patients with ventricular septal defect, namely, those with aortic insufficiency

In many if not most patients with ventricular septal defects there may be some degree of aortic insufficiency, which will vary from a smidgen to a sizable stream. Usually this can be ignored. It is not clinically detectable, and simply bothers the surgeon when he is attempting to repair the defect.

When there is significant clinical aortic insufficiency, however, we believe that the basic mechanism is that shown in this first slide (slide), namely, a prolapse of the right coronary cusp, shown here, and possibly a segment of the adjacent noncoronary cusp.

We have not been successful in attempting to coapt the commissures in these patients, and believe that, although the original trouble probably arises from the prolapse of the base of the leaflet, that the trouble we need to treat is in the greater length of the free edge, which actually prolapses beneath the adjacent cusp.

(Slide) We have treated this, as shown here, by simply reefing the free edge, in 3 patients, with excellent results in 2. I think the movie will show a specimen from the third patient. We obtained this specimen because I was, perhaps, obsessed with the idea that one could treat this by narrowing the aortic annulus, closing the defect in an improper fashion. This partially reopened, and the patient died of insufficiency.

I think this specimen demonstrates that the important phenomenon is reefing the free edge. This is viewed through a Lucite chamber in which water is put upon the valve, so that the pressure is constantly equal to the systolic pressure, and the valve is kept sealed. You notice that the cusps are at least together.

Here is the reefing. Here are sutures used below to close the ventricular septal defect. The sutures are removed, and you see that it makes no difference, really, in the competence of the aortic closure. This patient had a normal blood pressure after closure, and for a day and a half; then the pressure increased—I believe because of the tear in the base of the leaflet through which you saw the clamp come then.

Now, you will notice that the cusp had prolapsed down beneath the adjacent cusp. Notice how thin the base of this leaflet is where it has prolapsed through the ventricular defect. It does very little good to close the defect and buttress up the base of the valve. Again, the trouble is in the free edge.

(Slide) Here is the specimen after it has been fixed, so that the nearly normal arrangement can be seen. Here is the right coronary cusp prolapsing through the defect. Actually, at operation this almost sealed off the defect, so that there was very little leakage of blood through it. Notice how this has actually become detached from the edge of the ventricular defect.

Looking at this from above again, notice how the valve prolapses down, because of lengthening of the free edge. The difficult thing is to determine how much reefing one should do, and what we have done is to measure the diameter of the aorta with the aorta distended before we open the heart, and then to measure the length of the free edge of the cusp, and it is easy to see, on working with the valves, that the length of any free edge should be approximately the same as the diameter of the aorta, if the confluence of the cusps in the center of the aorta is to be obtained.

DR. EARLE B. KAY, Cleveland, Ohio.—We have been very pleased with the results obtained in the surgical correction of ventricular septal defects in a series of nearly 100 patients operated upon during the past 4½ years. Until recently we have had no deaths in any patient with pulmonary hypertension below 75 mm. Hg. About 2 months ago we had our first death in this group as a result of a staphylococcus-resistant infection.

During the past 3 years no patients have died, except for this one just discussed, regardless of the degree of pulmonary hypertension as long as there was still a left-to-right shunt. We have not operated on any patients with Eisenmenger's syndrome.

During the 4½ years that comprise this experience, there has been no instance of complete heart block. There were three temporary heart blocks that were immediately converted with Isuprel during the period of re-establishing the heartbeat at the conclusion of the surgical correction. We have not operated upon patients under 1 year of age, and, as far as I know, no patients have died during the last several years with conservative treatment during this early period of infancy. In any event, it is our opinion that the risk of medical management during the first year of life carries a lower mortality than when attempts at surgical correction are made.

Initially, we did not employ cardiac arrest, but during the past 3½ years probably over 90 per cent of the patients have had cardiac arrest with potassium chloride. Over 90 per cent of the patients have had closure of ventricular septal defect using a compressed Ivalon patch with interrupted silk sutures. We have been very careful in taking multiple small bites around the ventricular septum and probably this is the reason that we have not encountered any evidence of heart block.

We have had five recurrences during this time, all occurring during the first year. The first two were as a result of using non-compressed Ivalon, in which the pores increased in size. The other two were in patients who had closure without an Ivalon prosthesis. The fifth was in a patient with a Swiss cheese type of defect.

All 5 patients have now been reoperated upon. Four of the defects are completely closed, and the 1 patient with the Swiss cheese type of defect still has some partial opening.

DR. KIRKLIN (Closing).—Certainly, Dr. Bahnson has demonstrated better than anyone previously the anatomy of aortic incompetence in patients with ventricular septal defect. We can confirm his belief that it does no good merely to repair the ventricular septal defect. In the first case that we had some time back, we merely repaired the ventricular defect, thinking that that would push the aortic leaflet up where it should be and relieve the incompetence. The patient has survived, but still has a significant aortic valve incompetence.

I can only envy Dr. Kay and his results, and perhaps differ with him in one small point. I doubt that we can confidently assume that conservative management for the sick small infant in heart failure from ventricular septal defect will allow us to operate on him at the age of 2 years. In 1957 we banded some of these infants and treated some of them medically. Dr. DuShane in our clinic treated them carefully and diligently. Twenty-eight per cent of that small group died before they reached the age of 1 year. They did not die in failure in the hospital. Usually they went home, suddenly acquired a respiratory infection, and had overwhelming bronchopneumonia before they could be returned to the hospital.

DR. BRUCE JOHNSTON, San Francisco, Calif.—The few remarks which I have to make are merely to reinforce, I hope, the thesis which Dr. Morrow has so well developed.

There are several reasons why we have adopted extracorporeal circulation as the technique to allow us to repair secundum defects, but they are all linked essentially with the fact that we do not feel that the 6 or 8 minutes which hypothermia alone will give us is adequate in our hands for a satisfactory repair.

We have an early experience with some 40 cases which we closed by the external suture technique, and in 5 of these patients there was a very large residual shunt. They were all adults. The defect at the time of the first operation had always been large, and this indicated quite clearly to us that a certain number of these secundum defects would require some prosthesis in order to assure complete correction.

Furthermore, we find that in our series some 12 per cent of patients have anomalous venous return. Admittedly, a small number of these patients can have a correction performed without inserting a prosthesis, but the majority certainly do require a patch.

In all, we find that 10 per cent of our patients needed a patch of some sort. And so, for the last 104 patients we have used extracorporeal circulation, and with the most recent 45 patients we have used the lung recently described by Osborne, Bramson, and Gerbode.

We have had one death in this group of 104 patients, a child who was in severe cardiac failure at the time of operation, and we have good reason to believe that all the others are satisfactorily corrected.

DR GEORGE H. A CLOWES, JR, Cleveland, Ohio—Dr Morrow has just emphasized the need for doing very accurate surgery, for one reason—that is, to effect a complete repair Dr Scannell and other speakers this morning have talked about the quality of the repair of a valve and the dangers of regurgitation I would simply like to emphasize why it is that certain people produce beautiful results by rendering the heart capable of responding in normal fashion to the trauma of operation

(Slide) The cardiac output during the immediate postoperative period seems to follow a pattern in patients after thoracotomy. You will notice that there is a tremendous rise of cardiac output at the time the endotracheal tube is removed and, if the cardiac output goes up then, one can be sure that the patient will do well postoperatively During the first week the cardiac index remains about 30 per cent above the basal value Note that the venous pressure is up only during the period of the operation and the anesthesia

(Slide) Now, for comparison here is a series of 13 patients who had cardiac operations, studied in the same fashion, who survived Notice that they started with a lower cardiac index, but it came up at the time of extubation Their cardiac output actually went up after the cardiotomy had been completed Then there was a short period of depression during the first few hours Thereafter it remained up as in the rest of the thoracotomies

(Slide) This will show you the behavior of 6 patients who died Four of these were patients who had cardiac operations, one of them being an aortic valve procedure The cardiac output started with a low level, went down during the period of operation, but failed to go up at the end of the operation Not one of these patients reached the preoperative index

Dr Boyd and his associates from Johns Hopkins showed the same thing last year, and other people have emphasized this, but I believe this will serve to emphasize why we must do a complete repair on these various cardiac abnormalities If the myocardium is damaged by failure to perfuse the coronaries, or for other reasons, then we see a similar situation Patients who fail to respond in this normal fashion die in a state of metabolic acidosis

DR HENRY SWAN, II, Denver, Colo—We have continued to use the open closure of atrial septal defects with hypothermia alone, and we have had experience now with about 165 patients in whom this operation has been done

We also agree with Dr Johnston that about 12 or 13 per cent of these patients have some aberrant drainage of some type, usually associated with the very high, or sinus venosa, defect We have had 22 such patients

We have used hypothermia at 30° C rectal temperature We limit our occlusion period strictly to 6 minutes, and will not exceed that amount of time, but we do not hesitate to do two or three occlusions, and thus one can get 15 or 18 minutes of operating time, if so desired

In our last 125 patients we have had one death

The results have been documented by postoperative catheterization in 44 patients, largely in the earlier part of the series, as Dr Blount is no longer doing postoperative catheterization routinely in this type of patient Five of those 44 patients had evidence of failure to close completely the defect Two of these were in the early group of patients when we were using interrupted sutures, and I think I spaced the sutures too far apart Both patients were reoperated upon, and the residual hole was closed

One was known at operation to have been left with a vein which was untransposed, so it was no surprise to find some residual shunt in that patient

Two were actual failures of the technique One of these was an adult patient with a very large heart and a very large hole, measuring 9 cm, and I feel that in this patient there was a complete breakdown of the suture line An attempt was made to close it using cardiopulmonary bypass at another institution later on, but the patient failed to survive the procedure

I feel that we could quite agree with you that in the adult patient with the very large hole we may well need to put in prosthetic devices, but so far at least in our experience we have not used any prosthetic devices, and we think that it is quite possible to get accurate, successful closure at a very low risk using this technique

DR MORROW (Closing).—The object of one of these intracardiac exercises is to close the hole completely We are not satisfied with any residual shunt after an open operation, and I don t think that we can detect small shunts by the conventional methods

For example, among those patients undergoing postoperative catheterization a year or two ago, the oxygen method was being used in our laboratory at that time as well as the N_2O test Four of 8 such patients had no detectable shunt using the conventional methods, but the residual shunt was demonstrated by the inert gas test

With the open operation with bypass I think that Dr Gilbert and I would probably use a prosthesis now in 4 out of 5 patients with atrial septal defect, and our average perfusion time in an adult with an atrial septal defect approximates 45 minutes

DR FRANK GERBODE, San Francisco, Calif —Our early experience with potassium arrest taught us one thing, that it was advantageous to operate upon the quiet heart However, in the past 18 months we have not used potassium arrest, and have turned to using general body hypothermia in combination with extracorporeal circulation, and during the past year we have used this technique in over 200 open heart operations

General body cooling has been accomplished with the use of a new, very efficient heat exchanging lung (slide), which was developed in our laboratories with the help of M L Bramson and Dr John Osborn Our lung has a relatively low priming volume, and has the entire casing of the inside of the lung free and exposed to a water jacket This is a very efficient heat exchanging unit, and it doesn t require any separate cleaning, because it is isolated from the blood circulation

We have employed various degrees of hypothermia in combination with extracorporeal circulation, and, as you can see, the vast majority of patients have been only slightly cooled, and ventricular fibrillation has not been induced

However, for the more serious types of lesion with various types of acquired heart disease and tetralogy of Fallot, arrest has been induced by general hypothermia low enough to induce ventricular fibrillation This permits a lower flow than is necessary under normothermic conditions

This slide shows the rapidity with which a large patient can be cooled using this device Rewarming is slightly slower, of necessity

(Slide) We believe, too, that left atrial decompression is an absolute necessity for any patient who has a heart stopped by cold fibrillation or cold arrest We first used an entry through the left atrial appendage but found this rather difficult to manage, and have now, in the last year, employed a catheter placed posteriorly in the portion of the left atrium which presents on the right side If one passes a catheter through this area, you can in some instances thread it through the mitral valve and simultaneously decompress the left ventricle as well This is put in place in the early part of the perfusion, and it stays there until the heart stabilizes on coming off the pump

I believe the combination of general hypothermia with induced ventricular fibrillation with cold has resulted in patients who are metabolically better off during the postoperative period We have documented this in various ways, but it has also been clinically apparent to all of us As an example of the effectiveness of the technique, there were two operative deaths in the last 16 operations for cyanotic tetralogy

DR BENSON B ROE, San Francisco Calif —We have enjoyed the technical and clinical advantages of both general and regional hypothermia in conjunction with our *perfusions*, and I think with considerable advantage to the patient as Dr Gerbode indicated Indeed, I think that we could say that our postoperative pattern of acidosis has been converted to one of alkalosis

I rise principally to submit a simplified technique which has versatility and which permits the use of a single heat exchanger for both cooling and warming, and for both regional and general hypothermia.

The first slide demonstrates the method we now use routinely, which permits us to decide whether regional hypothermia is necessary during the procedure without necessitating additional equipment. This is our heat exchanger set up with the clamp placed here, so that from the reservoir source a single pump carries the blood through the heat exchanger for general body perfusion to control body temperature which is routinely lowered to 30° C. or lower.

If cardiac arrest is desirable, then this ''Y'' in the system is opened and the already cooled circulation is then partially shunted past the heat exchanger for continued body perfusion. A smaller portion of the same pump output passes through the other side of the ''Y,'' through the heat exchanger (now connected to an ice water tank) and thence into the coronary perfusion. The clamp can be reshifted for body warming afterward.

(Slide) This is a ''saddle'' needle which rests like a saddle over the aorta, with a curved needle designed to lie inside the ascending aorta, without harming the valve or piercing the posterior wall.

(Slide) This slide shows it in place. It is tied with a piece of umbilical tape around the aorta and across the saddle, and lies unattended out of the operative field.

DR. DONALD B. EFFLER, Cleveland, Ohio.—Scientific papers can be like old love letters in that the context written in all sincerity may be embarrassing when read years later.

On previous occasions, there have been references to a paper presented by Dr. F. Mason Sones, Jr., a member of the Department of Cardiology at the Cleveland Clinic. In this paper Dr. Sones cited the occurrence of myocardial necrosis at autopsy in patients who had succumbed following our early efforts in open-heart surgery. At the time of that publication, we did not understand the problems relative to fatal metabolic acidosis or the hazards of low flow perfusion; nor did we realize the myocardial changes that would occur in patients who had gross overdistention of the ventricles and the attendant damage to the pulmonary venous bed. The myocardial damage described in that paper is no longer a frequent finding in patients who do not survive operation whether cardiac arrest was employed or not. For the record I believe that we should deal with present knowledge rather than a misconception published almost 4 years ago.

Perhaps I have been stubborn in my continued use of elective cardiac arrest utilizing potassium citrate. It is still a very useful adjunct in surgery that utilizes extracorporeal circulation, but must be used properly and in selected cases. As we have reported many times in the past, adults and children alike do tolerate potassium arrest for periods of time that may exceed 60 minutes.

I agree with the authors that regional hypothermia is an extremely valuable adjunct, particularly in surgery of the aortic valve; whereas our technical methods may differ slightly, the basic approach is quite similar. I would like to emphasize again, however, the necessity for proper and adequate left heart decompression while the isolated heart is reperfused, and in particular during the rewarming period before the left ventricle has regained its proper tone.

Ventricular fibrillation is almost invariably seen in patients who have had cold arrest. In patients who have had severe rheumatic heart disease with marked myocardial damage and enlargement, this can be a real problem in resuscitation. In an earlier paper Dr. Harken mentioned 1 case in which electric shock was employed over 20 times in an effort to convert ventricular fibrillation to an effective rhythm. Our experience has been similar and for this reason we make no effort to defibrillate the heart until we have brought its temperature back to a comparatively normal level. If ventricular fibrillation is still persistent, we have employed one small trick that is worthy of mention and that is the use of quinidine sulfate. Quinidine sulfate may be given by the Melrose technique, and its action can be very prompt. We have employed it in large doses on occasion by direct injection into the extracorporeal circulation. When used in this manner, however, it may be conducive to rather severe hypotension even after an effective ventricular rhythm has been re-established.

DR. A SENNING, Stockholm, Sweden.—There have been some deaths reported from cerebral damage after this type of procedure, and therefore I wish to discuss the conditions of the brain temperature. The brain temperature is dependent on many factors, the most important being the perfusion technique used.

If we are using the femoral artery for the arterial cannulation and are using flows through the heat exchanger or through the pump that are significantly smaller than the cardiac output, then the upper part of the body, including the brain, is perfused by "warm" blood from the heart itself.

(Slide) This slide shows an experiment where we have had a rather low flow through the double pumps and the heart has been in good action. The temperature in the brain is shown here (indicating), and the one in the esophagus and rectum are shown here.

The temperature in the brain falls very slowly compared to the temperature in other organs up to this point here, where the heart stops. At this point there is a difference in temperature of 12° C. Then the brain temperature also falls rather rapidly, but still here when it's 10° or 11° C. in the esophagus and the rectum, there is a temperature of about 20° C. in the brain.

(Slide) The next slide shows more or less the same as Dr. Gordon showed us in his excellent presentation. In this experiment the temperatures in the esophagus and the rectum have fallen to about 12° C., but the temperature in the brain is still 22° C. During an induced circulatory arrest (this time it was 50 minutes), the temperature in the brain goes up from 22° to 25.6° C. I don't think that a patient in similar condition could stand a cardiac arrest of 40 minutes.

We have to be aware of the possible difference in temperature between brain and esophagus and the rise in temperature during circulatory arrest.

DR. ROLLINS HANLON, St. Louis, Mo.—My comments are applicable to the last two papers; namely, selective hypothermia in cardiac arrest as contrasted with generalized hypothermia.

One of the reasons for uncertainty about the innocuousness of cardiac arrest has been the lack of critical assessment of cardiac function after arrest and ischemia. Studies which have been done by Dr. Willman and Dr. Howard and others in our laboratory bear on this problem.

(Slide) These are left ventricular function curves, with the upper curve showing function in the control period before hypothermic arrest. After arrest of the heart for 30 minutes in the dog, you can see that the ventricular function curve shows considerable depression of left ventricular stroke work in gram-meters. The temperature of the heart has been lowered to the point of arrest by the perfusion with cold blood, but with cessation of perfusion the temperature of the heart has drifted upward, as was emphasized by Dr. Gordon. With this elevation, the heart goes into ventricular fibrillation, followed by arrest; that is essentially anoxic arrest. Hence mere arrest by cold blood with subsequent rise in temperature exposes the heart to the same damaging effects that one gets, theoretically at least, from anoxic arrest.

(Slide) In contrast, if one attempts to keep the temperature of the heart down by internal and external lavage with cold solutions, you can see that ventricular function is good after arrest, although not as good as in the control period. This is a matter of how efficiently one cools the heart locally.

(Slide) The final slide indicates the use of total body hypothermia, so that the temperature of the heart really remains at 15° C. Under these circumstances with 30 minutes of arrest, the ventricular function after rewarming shows a curve that closely approximates the control value.

We would like to stress the fact that if one stops the heart by local hypothermia, unless that cardiac hypothermia is maintained, the deleterious effects of anoxic arrest will become manifest.

DR. JOHN Y. TEMPLETON, Philadelphia, Pa.—We have done some work in the laboratory, as have many of you, I'm sure, with double pumps and the heat exchanger. We have, in general, used, I think, a flow which is probably somewhat larger than Dr. Gordon's having maintained it by addition of blood as required, and with this method the decrease in over-all body temperature is considerably greater. For example, muscle temperatures are somewhat lower than he has stated here.

I should like to show one slide (slide) to point out something about the carbon dioxide in this type of preparation. When one is using the intact lungs, one is using a gas exchanger which is a great deal more efficient than those which we are accustomed to use in the heart-lung bypass. This is an adult female patient who had an atrial septal defect, and was cooled to only 20° C. with this method. You will observe the very significant fall in the partial pressure carbon dioxide in the arterial blood, and the rise in the pH; this in spite of the fact that during this cooling period the patient was ventilated using a non-rebreathing system with 3 per cent carbon dioxide in air. You will notice that the PCO_2 of the arterial blood is quite close to the PCO_2 of the inspired air.

DR. GORDON (Closing).—There are many more questions which could be raised regarding the clinical application of deep hypothermia. Our own investigations in this area are continuing in an effort to resolve some of the remaining problems.

Early in our deep hypothermia experience we were concerned with the possibility of central nervous system damage. However, studies on over 60 dogs subjected to prolonged periods of circulatory arrest under deep hypothermia failed to reveal central nervous system damage when the duration of circulatory arrest did not exceed the limits defined in this report. Our experiences have been the same with the patients in this series. The absence of postoperative electroencephalographic changes, the absence of neurological findings, and the absence of behavior changes in these patients indicates to us that the central nervous system has been protected adequately.

As regards brain temperature, our experiments in dogs reveal that the esophageal and brain temperature parallel each other closely when the thermistor probes are properly placed. During circulatory occlusion, the brain temperature drifts up less than the esophageal. This probably results from the esophagus being surrounded by a large mass of warmer muscle and subcutaneous tissues, whereas, the brain is isolated and retains its temperature better.

Anesthesia is not required when the patient's temperature drops below 28° C. We have used 5 per cent carbon dioxide and 95 per cent oxygen as the inhalant during cooling and rewarming. There are a number of reasons which can be advanced for this use of carbon dioxide. Our primary reason is that, in the hyperventilated patient, the addition of carbon dioxide tends to preserve the base bicarbonate. This is important because there is always some degree of metabolic acidosis following rewarming.

At the completion of rewarming the mixed venous pH is usually in the range of 7.28. When an adequate blood pressure is maintained the pH is usually back to normal within 8 hours. None of these patients has required intravenous bicarbonate or lactate postoperatively to combat acidosis.

I hope that by the time of this meeting next year, many of you will have used deep hypothermia for intracardiac surgery and that we will have an opportunity to compare our experiences at that time.

MYOCARDIAL DYSFUNCTION AFTER CARDIOPLEGIA

An Experimental Study

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Today cardioplegia achieved with potassium citrate (the Melrose technique)[1, 2] is condemned as vociferously as it was enthusiastically acclaimed 4 years ago. Other cardioplegic agents and techniques have since been introduced and in turn received with varying degrees of enthusiasm. We share the clinical impression with others that induced cardiac arrest has often produced serious impairment of myocardial function. However, hypotension and circulatory failure cannot be ascribed solely to cardioplegia. The ventriculotomy and the hemodynamic adjustment required of the heart are important determinants. Because of the many factors involved in the success of a complicated open-heart procedure, the survival of the animal or patient has proved to be an unreliable or inadequate measure of the safety and relative value of a cardioplegic agent. Our investigation was undertaken in order more accurately to evaluate and quantitate different methods of elective cardiac arrest.

Sarnoff and Berglund[3] have shown that ventricular performance can be expressed as a function curve in which ventricular stroke work is plotted against the corresponding mean atrial or ventricular filling pressure. In their experiments, which did not involve extracorporeal circulation, the data were obtained by progressively elevating the atrial pressure with increments of blood transfused into the experimental animal. The resulting cardiac output was measured by means of a flow meter. Stirling, Stanley, and Lillehei[4] studied the effects of ventriculotomy upon right ventricular function using Sarnoff curves. They collected the necessary data by controlled venous inflow. We have employed a similar technique in our own studies.

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METHODS

Twenty-six mongrel dogs, averaging 9.5 Kg., were medicated with 4 mg. per kilogram morphine sulfate and anesthetized with alpha-chloralose and urethane, after induction with Pentothal sodium. Heparin was the anticoagulant used, 5 mg. per kilogram. Extracorporeal circulation with total perfusion was established for 15 minutes with a rotary pump and homologous lung oxygenator (Fig. 1). The perfusion circuit was then modified for controlled venous inflow and, at increasing flow rates from 600 to 3,000 c.c. per minute, the mean right atrial, pulmonary artery, left atrial and aortic pressures were recorded. With pressures converted to centimeters of water, the following formulas yield ventricular stroke work:

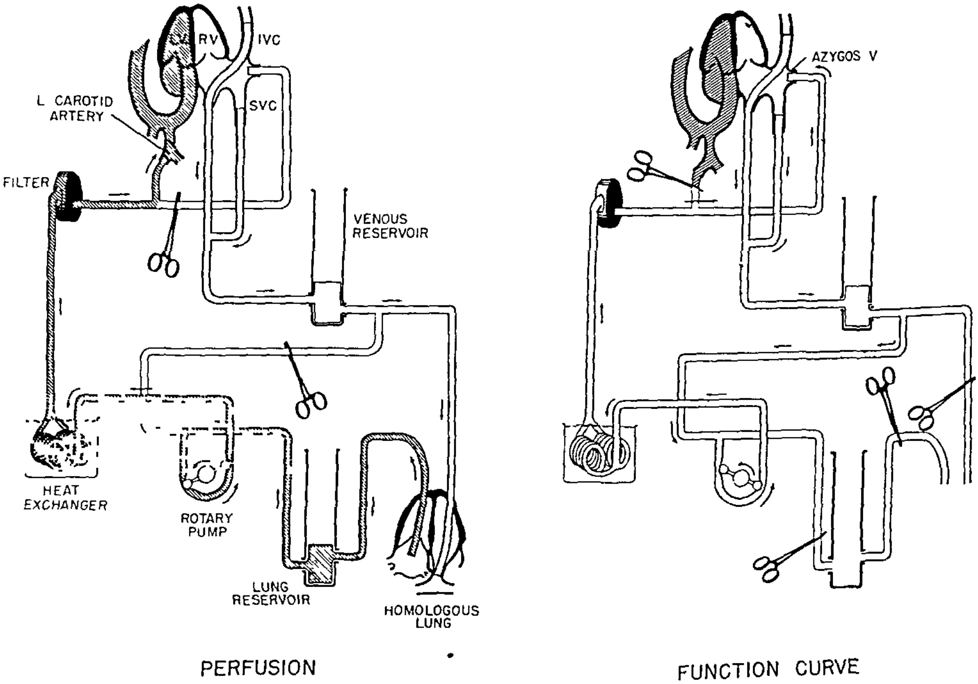

Fig. 1.

$$\text{RV stroke work (Gm.-meters)} = \frac{\text{Flow (c.c./min.)} \times (\text{PA} - \text{RA pressure})}{\text{Pulse rate} \times 100}.$$

$$\text{LV stroke work (Gm.-meters)} = \frac{\text{Flow (c.c./min.)} \times (\text{Ao} - \text{LA pressure})}{\text{Pulse rate} \times 100}.$$

All function curves were determined at 35° C. The average maximum control stroke work for all left ventricles was 28.8 Gm.-meters, and for all right ventricles was 5.2 Gm.-meters. Function curves for each normal ventricle were constructed by plotting each filling pressure (mean atrial pressure) against the stroke work which it produced (Curves I for Figs. 2, 3, 4).

Total perfusion was then reinstituted and the heart arrested by one of the five techniques described later. After a 15-minute period of cardiac depression or arrest the heart was released and cardiac action resumed (with defibrillation in 2 cases). Both atria were decompressed until cardiac action was adequate to prevent distention of the heart. Function (Curve II) was studied after 15 minutes of recovery perfusion, and again (Curve III) after an additional perfusion of 15 minutes (approximately 1 hour after arrest).

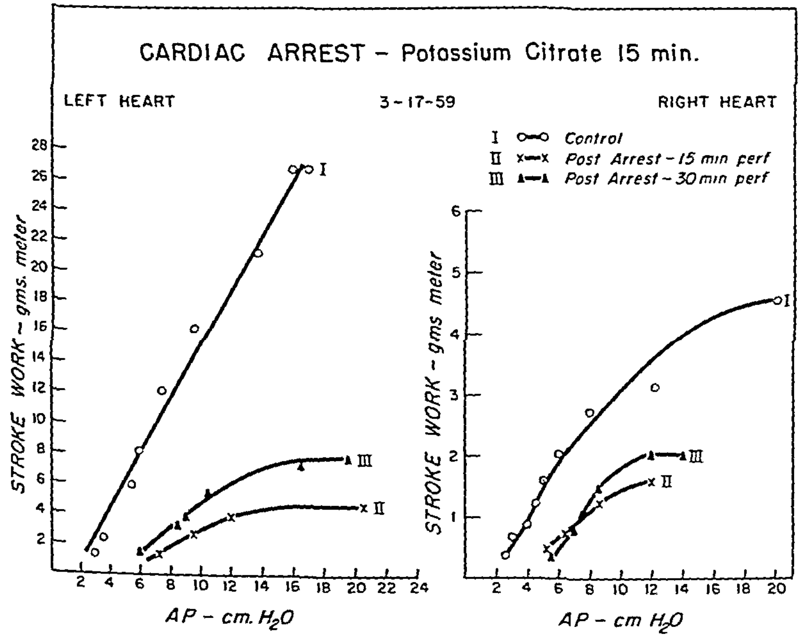

Fig. 2.

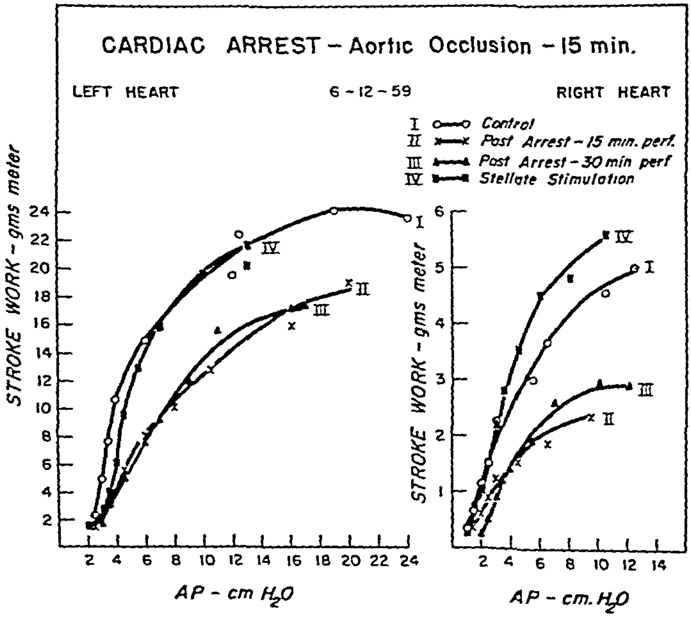

Fig. 3.

(In some experiments the effect of stimulating the isolated right stellate ganglion was evaluated [Curve IV].) The function curves thus obtained were then plotted together to form a family of curves produced by a single heart (Figs. 2, 3, 4).

Heretofore function curves of variously treated hearts have been compared by gross visual impression in regard to maximum peak, slope, and displacement along the abscissa.[1-6] This comparison "by impression" does not allow statistical integration of several experiments. Every function curve represents its heart's functional capacity over the wide range of filling pressures by which it might be challenged. It is impossible by any single formula to assign to every function curve a numerical value which is quantitatively significant of function. However, the relative values of two curves in the same family may be expressed numerically as the average ratio between their stroke works over a range of atrial pressures. This average ratio is accurately expressed by relating the areas under curves delimited by properly selected ordinates (Fig. 5). In these experiments control curves are considered 100 per cent of ventricular function, and post-arrest curves are related to the control curves in terms of per cent.

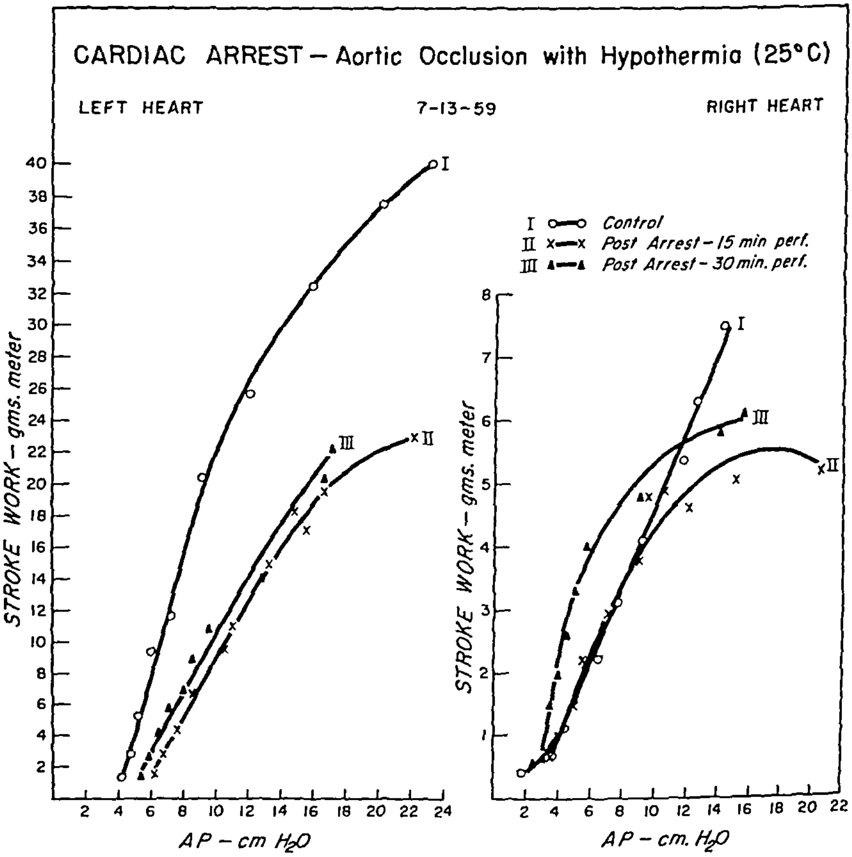

Fig. 4.

RESULTS

Acetylcholine (10 mg./Kg.) achieved arrest promptly when injected into the proximal, clamped aorta of normothermic dogs. In 3 dogs the aorta was released after a 3-minute arrest, and in 4 dogs arrest was maintained for 15 minutes. Cardiac contraction returned promptly upon release of the aorta in all cases. Post-arrest function curves are expressed as per cent of control function as shown in Table I. The average values for per cent function shown in Table I are plotted in Fig. 6. Significant is the finding that marked depression of both ventricles occurs after acetylcholine arrest of either duration, but a more rapid recovery is found after the shorter arrest (Fig. 6).

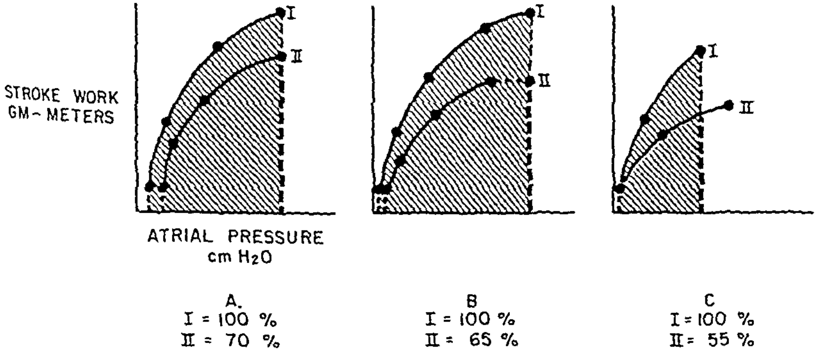

Fig. 5—Hypothetical function curves demonstrating method of deriving curve area and per cent of function.

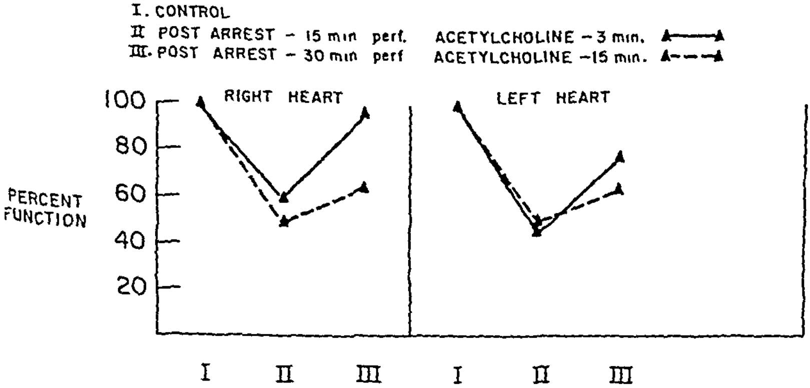

Fig 6—Delayed recovery of ventricular function by prolonged cardiac arrest.

Potassium citrate (2.5 per cent) produced immediate arrest in 7 normothermic dogs. In 3 animals, the aorta was released after a 3-minute arrest, while in 4 the arrest was maintained for 15 minutes. In all cases cardiac action resumed promptly. Function curves derived from these experiments were converted to areas and per cent of controls, and results are shown in Table II. Technical errors in the 3-minute arrest experiments produced inexplicable results, while 15-minute arrest experiments resulted in marked depression of both ventricles with partial, but very incomplete, recovery

TABLE I. ACETYLCHOLINE CARDIOPLEGIA

EXPERIMENT NUMBER	MAXIMUM STROKE WORK (GM.-METERS)						PER CENT FUNCTION					
	RIGHT			LEFT			RIGHT			LEFT		
	I	II	III	I	II	III	I	II	III	I	II	III
AC-3 min-1	3.5	3.9	4.4	30.0	25.1	24.6	100	100	112	100	79	79
AC-3 min-2	5.3	3.9	4.6	23.9	10.3	13.3	100	38	67	100	36	54
AC-3 min-3	4.0	3.2	3.7	22.2	13.4	16.0	100	45	110	100	27	103
AC-3 min-Aver.	4.3	3.7	4.2	25.4	16.2	18.0	100	61	96	100	47	78
AC-15 min-1	3.2	1.5	2.0	27.1	12.5	11.1	100	25	38	100	18	25
AC-15 min-2	6.6	3.7	5.1	25.2	16.5	19.4	100	45	76	100	24	53
AC-15 min-3	2.6	1.2	2.1	21.4	15.4	20.0	100	72	86	100	86	94
AC-15 min-4	5.0	3.2	3.0	24.6	14.0	19.8	100	59	59	100	60	85
AC-15 min-Aver.	4.4	2.4	3.1	24.6	16.6	17.6	100	50	64	100	50	64

Calculations of integrated areas are available from the authors upon request.

occurring during the 15-minute additional perfusion. The results of Experiment KC-15-2 are plotted in Fig. 2 as an example of this severe myocardial depression.

TABLE II. POTASSIUM CITRATE CARDIOPLEGIA

EXPERIMENT NUMBER	MAXIMUM STROKE WORK (GM.-METERS)						PER CENT FUNCTION					
	RIGHT			LEFT			RIGHT			LEFT		
	I	II	III	I	II	III	I	II	III	I	II	III
KC-3 min-1	4.4	3.7	3.2	31.2	24.2	21.3	100	83	74	100	74	57
KC-3 min-2	4.1	5.1	4.9	40.0	28.6	28.5	100	144	83	100	75	54
KC-3 min-3	4.1	3.7	3.1	20.5	19.8	19.3	100	97	90	100	76	92
KC-3 min-Aver.	4.2	4.1	3.7	30.6	20.9	23.0	100	108	82	100	75	68
KC-15 min-1	3.4	4.0	2.9	22.6	21.4	28.2	100	86	80	100	54	127
KC-15 min-2	4.5	1.6	2.0	26.8	4.5	7.7	100	38	47	100	16	19
KC-15 min-3	5.1	4.7	4.5	33.3	28.2	28.4	100	90	97	100	86	90
KC-15 min-4	3.3	2.0	2.9	26.4	15.8	18.7	100	54	88	100	52	68
KC-15 min-Aver.	4.1	3.1	3.1	27.2	17.8	20.8	100	67	78	100	52	76

Hypoxic arrest was achieved by simple aortic occlusion in 4 normothermic dogs. Cardiac action ceased on an average of 6 minutes after occlusion. After 15 minutes of occlusion, the aorta was released and cardiac action resumed spontaneously in 3 hearts. In the fourth heart, electrical defibrillation was easily accomplished. Table III shows conversion of post-arrest function curves

TABLE III. HYPOXIA (AORTIC OCCLUSION)

EXPERIMENT NUMBER	MAXIMUM STROKE WORK (GM.-METERS)						PER CENT FUNCTION					
	RIGHT			LEFT			RIGHT			LEFT		
	I	II	III	I	II	III	I	II	III	I	II	III
X-15 min-1*	3.6	0.9	0.9	38.0	10.7	6.7	100	29	25	100	28	20
X-15 min-2	5.0	2.4	3.0	24.2	19.0	17.5	100	52	60	100	67	68
X-15 min-3	5.6	3.1	3.4	29.1	24.4	32.1	100	50	54	100	69	104
X-15 min-4	8.6	3.8	5.6	26.9	10.3	17.2	100	48	66	100	32	34
X-15 Aver.	5.7	2.6	3.2	29.6	16.1	18.6	100	45	51	100	49	55

*Electrical defibrillation.

to per cent of control function. Ventricular depression occurred in the same range as following 15-minute arrest by acetylcholine and potassium citrate. It should be noted, however, that the hypoxic arrested hearts were quiet for an average of only 9 minutes, and recovery from hypoxic arrest is more delayed than that following arrest by the drugs tested. Experiment X-15-2 is plotted in Fig. 3 as an example of myocardial depression from hypoxic arrest.

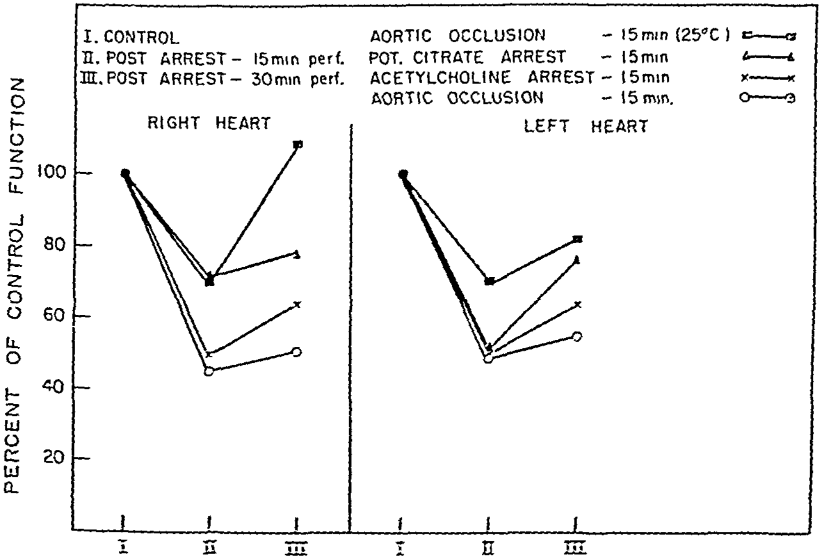

Fig. 7.—Ventricular function following cardioplegia.

Aortic occlusion at 25° C. for 15 minutes (during which time the animal was rewarmed and the heart remained below 29° C.) was performed in 4 experiments. As in the other experiments, myocardial function was measured at 35° C. In each case the heart moved quietly until release of the aorta, when good cardiac action resumed immediately. Post-arrest function curves were converted to per cent of control of function (Table IV). In this series of experiments, both ventricles showed less depression and more rapid recovery than was found in any of the three previously tested methods of cardioplegia. Fig. 4 illustrates the favorable influence of hypothermia as determined in Experiment 25-15-2

Table IV. [illegible] at 25° C.

Experiment Number	[illegible] Right I	II	III	Left I	II	III	Per cent of control function Right I	II	III	Left I	II	III
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	22.2	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Results of the four techniques considered thus far are summarized in Fig. 7. Approximately 50 per cent loss of function occurs in both ventricles after 15-minute cardioplegia by each technique except for aortic occlusion at 25° C., where 70 per cent of function is retained by both ventricles. After an additional 15-minute perfusion, further recovery occurs in all cases: to 51 per cent and 55 per cent in the right and left ventricles, respectively, after simple aortic occlusion, 64 per cent and 64 per cent after acetylcholine, 78 per cent and 76 per cent after potassium citrate, and 108 per cent and 82 per cent after hypthermic aortic occlusion. The last method appears to be the least harmful.

Sympathetic stimulation: In 12 dogs, a fourth function curve was derived immediately after obtaining Curve III (on an average of 80 minutes postarrest). During this phase of the experiment, the isolated right stellate ganglion was stimulated continuously with 20 to 30 volts at 25 cycles per second. The purpose of this maneuver was to determine whether elective cardiac arrest impaired the heart's responsiveness to sympathetic stimulation. In 75 per cent of cases (see Fig. 3), Curve IV revealed improvement over Curve III but, because control stimulation curves were not made, it is not known whether the additional improvement was spontaneous or induced. More conclusive studies are now in progress.

Total body hypothermia to 15° C. with interruption of perfusion for 15 minutes was performed in 3 dogs. Cooling and rewarming was effected by a heat exchanger in the extracorporeal circuit. In each experiment a quiet but tonic heart was produced, and in only 1 case was defibrillation necessary upon recovery. The results shown in Table V reveal wide discrepancies with a general tendency toward delayed loss of function. These findings may represent the delayed effect of hypothermia and rewarming. Since no metabolic studies were performed in this series of experiments, the data allow no conclusions.

TABLE V. HYPOTHERMIA (15°)

EXPERIMENT NUMBER	MAXIMUM STROKE WORK (GM.-METERS)						PER CENT FUNCTION					
	RIGHT			LEFT			RIGHT			LEFT		
	I	II	III	I	II	III	I	II	III	I	II	III
15-15-1	3.6	2.9	2.8	24.7	18.5	21.2	100	64	46	100	55	64
15-15-2*	2.8	4.2	4.3	18.9	15.5	16.5	100	142	139	100	101	102
15-15-3	9.8	2.7	7.8	23.3	14.2	12.0	100	59	52	100	56	28
15-15-Aver.	5.4	3.3	4.9	22.3	16.1	16.6	100	88.3	79.0	100	70.7	64.7

*Electrical defibrillation.

DISCUSSION

Investigations on cardioplegic agents have been carried out by a variety of methods. These include observations on the recovery and contractility of the isolated heart or on the isolated heart metabolically supported by a donor animal. Studies have been reported on the period of time for pump support following cardiac arrest in order to achieve a satisfactory and stabile arterial pressure. Other investigations concern the oxygen consumption of the arrested heart or the developing tissue acidosis. Survival statistics have been compared between animals undergoing cardiac arrest and those in which coronary perfusion was uninterrupted, or interrupted by simple aortic occlusion. Finally, histologic changes in the myocardium of surviving animals have been reported. As compared to these methods, ventricular function studies by the Sarnoff technique have the distinct advantage of stressing the heart to the point of maximum performance while allowing a rough quantitation of this performance. Moderate or even minor impairment of myocardial function is thus revealed.

In a series of recent reports, Hanlon and his associates[5, 6] have shown marked depression of left ventricular myocardial function after a 30-minute arrest with either potassium citrate, acetylcholine, a mixture of prostigmine, magnesium sulfate and potassium citrate, or aortic occlusion. There was reduction in maximum stroke work performance from the control value of 25 to 50 to less than 10 Gm.-meters of work, when measured 10 minutes or 2 hours post-arrest. Less depression was noted after potassium arrest for 20 minutes. Partial protection of the heart was provided by previous digitalization or cooling to 28° C., and partial recovery was effected by administration of Wyamine. Weirich, Jones, and Burke[7] have noted a similar effect on myocardial function with increasing deterioration as the period of arrest was prolonged from 5 to 20 minutes. The effect of potassium citrate, acetylcholine, or simple aortic occlusion was roughly the same.

Braunwald, Morrow, and their associates[8] found severe depression in myocardial function after 20 to 30 minutes of arrest with either potassium citrate or acetylcholine. Using intermittent aortic occlusion, however, with 4 minutes of occlusion and 1 minute of release alternately over a period of 30 minutes, they found no significant depression.

The ventricular function studies reported in this paper were commenced before the work of the above investigators was known to us. Our methods and our results are closely similar to those of these authors. However, a valid method of integrating the data of identical experiments has been devised, permitting us to compare statistically the results of any given type of arrest in a series of experiments (Fig. 5). The data obtained were thus analyzed and justify the following conclusions.

CONCLUSIONS

1. Cardiac arrest for 15 minutes by any of the techniques studied results in depression of myocardial function to 50 to 70 per cent of control function when measured 15 minutes post-arrest.

2. Partial recovery of myocardial function occurs with an additional 15-minute perfusion.

3. At normal body temperature, 15-minute cardiac arrest by potassium citrate and by acetylcholine, and 15-minute aortic occlusion, cause similar degrees of depression, although recovery appears to be most rapid after potassium citrate and most delayed after hypoxia.

4. Prolongation of cardioplegia results in greater depression of myocardial function, and further delay in recovery of function.

5. Hypothermia to 25° C. partially protects the heart rendered hypoxic for 15 minutes and, in comparison with other methods studied, cardioplegia by this technique resulted in least depression and best recovery of myocardial function.

We are indebted to Dr. Stanley J. Sarnoff for his suggestions which have aided in the conduct of these experiments and in the preparation of this manuscript.

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REFERENCES

1. Melrose, D. G., Dreyer B., Bentall, H. H., and Baker, J. B. E.: Elective Cardiac Arrest, Lancet 2: 21, 1955.
2. Baker, J. B. E., Bentall, H. H., Dreyer, B., and Melrose, D. G.: Arrest of Isolated Heart With Potassium Citrate, Lancet 2: 555, 1957.
3. Sarnoff, S. J., and Berglund, E.: Ventricular Function. I. Stirling's Law of the Heart Studied by Means of Simultaneous Right and Left Ventricular Function Curves in the Dog, Circulation 9: 706, 1954.
4. Stirling, G. R., Stanley, P. H., and Lillehei, C. W.: The Effects of Cardiac Bypass and Ventriculotomy Upon Right Ventricular Function, S. Forum 8: 433, 1957.
5. Cooper, T., Willman, V. L., Zafiracopoulos, P., and Hanlon, C. R.: Myocardial Function After Elective Cardiac Arrest During Hypothermia, Surg. Gynec. & Obst. 109: 423, 1959.
6. Willman, V. L., Cooper, T., Zafiracopoulos, P., and Hanlon, C. R.: Depression of Ventricular Function Following Elective Cardiac Arrest With Potassium Citrate, Surgery 46: 792, 1959.
7. Weirich, W. L., Jones, R. W., and Burke, M.: Effect of Induced Cardiac Arrest by Potassium Citrate and Acetylcholine on Ventricular Function. Presented at Clinical Congress, American College of Surgeons, Atlantic City, N. J., Sept. 29, 1959.
8. Braunwald, N. S., Waldhausen, J. A., Cornell, W. P., Bloodwell, R. D., and Morrow, A. G.: Left Ventricular Function Following Elective Cardiac Arrest. Presented at Scientific Session of the American Heart Association, Philadelphia, Pa., Oct. 23, 1959.

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